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MAIN CONTENTS:

	PAGES		PAGES
Leishmaniasis in Greece ...	1–7	Relapsing Fever and other Spirochaetoses	92–93
Exudate from Millipedes with Particular Reference to its Injurious Effects	7–12	Yaws	94–95
Summary of Recent Abstracts. I. Cholera	12–14	Leprosy	95–96
Malaria	15–44	Helminthiasis	96–113
Blackwater Fever	44–45	Deficiency Diseases	114–120
Trypanosomiasis	45–54	Sprue	120–121
Leishmaniasis	54–56	Haematology	121–122
Fevers of the Typhus Group...	56–71	Venoms and Antivenenes ...	122–123
Yellow Fever	71–75	Dermatology and Fungus Diseases	123–125
Plague	76–79	Heat Stroke and Allied Conditions	126–127
Cholera	79	Miscellaneous Diseases ...	128–130
Bacillary Dysentery	79–80	General Entomology ...	131–136
Amoebiasis and Intestinal Protozoal Infections ...	80–91	Laboratory Procedures ...	136–138
		Reports, Surveys and Miscellaneous Papers	138–144

For detailed Contents see pp. ii, iv, vi, viii, ix and x.

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

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LEISHMANIASIS IN GREECE.*

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In Greece human visceral leishmaniasis, canine leishmaniasis and oriental sore are endemic and, curiously enough, coexist, in some districts, at the same place.

Kala azar.—New foci are constantly being discovered. The widest endemic focus now seems to be in Messinia (ADAMOPOULOS, 1926; JOANNIDÈS, 1926; MATARANGAS, 1927; COPANARIS, 1935; PAPANTONAKIS, 1937) in the Peloponnese. Other cases from the Peloponnese are found in Argos (KIRIMLIDIS, 1938), villages of Argolis (KIRIMLIDIS, 1938), Nauplia (CARDAMATIS, 1912; KIRIMLIDIS, 1938), Patras (CARDAMATIS, 1912), in Poros (CAMINOPETROS, 1934) and the islands Spetsai and Hydra (CARDAMATIS, 1912; MATARANGAS, 1927; LIGNOS, 1932; COPANARIS, 1935) which are in the vicinity. Still other foci exist in the neighbourhood of Athens (CARDAMATIS, 1912; MATARANGAS, 1927; SPYROPOULOS, 1928; CAMINOPETROS, 1934; COPANARIS, 1935), Piraeus (CARDAMATIS, 1912) and Salamis (PANGALOS, 1929) and in the Ionian islands—Corfu, Cephalonia (DIWARIS, 1914), Ithaca and Paxoi. Inside and in the neighbourhood of Preveza (MATARANGAS, 1927), in Lamia (MATARANGAS, 1927), Thessaly—Volos, Trikkala, Almyros (CARDAMATIS, 1912; COPANARIS, 1935)—Macedonia—Salonika, Drama, Serres, Kavalla, as well as in villages of eastern Macedonia (ALEXANDRIDES, 1929)—and more especially in Crete—Canea, Lasithi (MATARANGAS, 1927; COPANARIS, 1935; PAPANTONAKIS, 1935, 1936; MAYER and MALAMOS, 1936; ADLER, THEODOR and WITENBERG, 1938).

Kala azar in Greece is a children's disease, as in other Mediterranean countries. Children are infected usually during the first four years of life, but we saw also cases in older children and even in adults. It is not rare to trace two or more cases of this disease in the same house. The clinical picture includes the familiar symptoms, namely: a persistent, atypical fever, great enlargement of the spleen and the liver, emaciation, hypochromic anaemia, leucopenia, sometimes a haemorrhagic diathesis of the skin and the mucous membranes, and dysenteric disorders. The dark pigmentation of the skin, which has given

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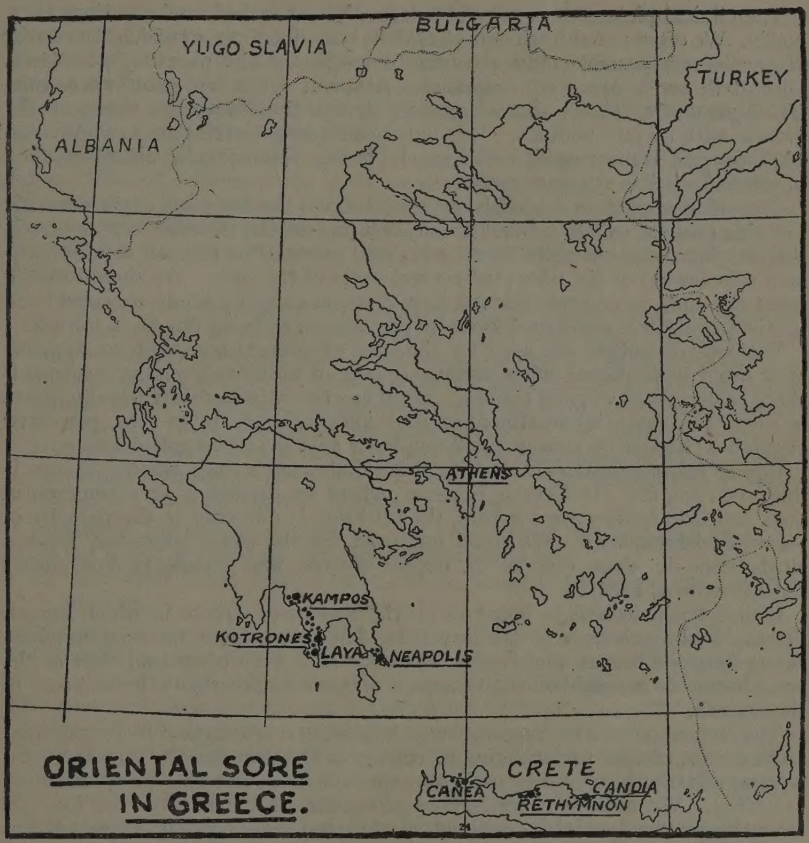
to the disease its name (kala azar—black disease or black death) did not occur in all our cases. It is strange to note that in some villages all the cases showed skin haemorrhages, and that in neighbouring villages not one with this haemorrhagic diathesis was encountered (MALAMOS, 1937). It is interesting also to note that in a case with a clinical appearance like Banti's syndrome, CAWADIAS, at the post-mortem examination, found the parasites not only in the spleen and the liver but also in the wall of the splenic vein.

Diagnosis is made by demonstration of *Leishmania donovani* by puncture with a syringe. Liver and lymph gland punctures are seldom used, and we prefer punctures of the spleen or the sternum. It must be emphasized that, often, in the bone-marrow a few parasites only were detected after long search, and that sometimes they were even absent. Most physicians use for spleen puncture the Aravantinos syringe, which has the advantage of quick withdrawal of the splenic tissue, owing to the adjusted spring which allows the automatic retraction of the piston. We favour less the serological diagnostic methods because of the more accurate results given by the detection of the *L. donovani*. Others favour the serologic methods and PHINOS (1932) prefers Chopra's test with a 4 per cent. Neostibosan solution, CAMINOPETROS (1934) his sulpharsenol test.



From the therapeutic point of view, in the cure of kala azar I must say that as in other Mediterranean countries, we use relatively higher doses of drugs than those used in Eastern Asia (PHINOS, 1932; MAYER and MALAMOS, 1936; MALAMOS, 1937).

Orien'al sore.—The skin manifestation of human leishmaniasis occurs more particularly in Crete (Department of Canea, Rethymnon, Candia) (COPANARIS, 1935; PAPANTONAKIS, 1935, 1936; MAYER & MALAMOS, 1936; MALAMOS, 1937; ADLER, THEODOR and WITENBERG, 1938) and also in Lakonia (in and around Neapolis, Kampos, Cotrones, Laya (JOANNIDÈS, 1926; BLANC and CAMINOPETROS, 1927)). Sporadic cases are found in various other districts of Greece and even in Athens (BLANC and CAMINOPETROS, 1928). In Crete and Lakonia, oriental sore often assumes an epidemic character, affecting the greater part of the population. As stated already, visceral leishmaniasis in Greece is always endemic; never epidemic.

Oriental sore is common to all ages, and affects more particularly the uncovered parts of the body: the face, the neck, the upper limbs; in women seldom the chest. The lower limbs are rarely affected in adults, but often in children. We had the opportunity to observe cases with only one sore, while in others one hundred or more sores could be found (DOUCAS, 1929).

The clinical picture does not differ from that described in the various text-books. We often noted fresh non-ulcerated, acne-like sores, of which the correct diagnosis was possible only after the detection of the parasite, *L. tropica*. Ulcerated sores are very common. Atypical sores are not uncommon (HIGOUMENAKIS, 1938). Sometimes we found the infiltrative form of the disease with miliary nodules. It is only after a long search that *L. tropica* can be discovered in most cases of this special form. Secondary bacillary infection of oriental sores is not uncommon.

The safest method of diagnosis of oriental sore is the detection of the parasite. For this purpose we use a small lancet, or a fine needle, in order to puncture in the peripheral regions of the sore. As is well known, it is difficult to find leishmania in tissues of the ulcerated central parts of the sore. We should like to point out that, in endemic regions, skin diseases of many kinds are considered by the population, sometimes even by physicians, as being due to *L. tropica*.

Various treatments are used for the cure of oriental sore, but, as happens very often in medicine, when there is a lack of uniformity in the treatment, there is also a lack of good results. Local emetine injections are usually given, or mepacrine (atebrin) treatment is used, and in Canea 10 per cent. powdered vegetable charcoal in concentrated sulphuric acid is often applied locally.

Canine leishmaniasis.—In east Asia, leishmaniasis in dogs, when it occurs, is due to *L. tropica*. In Greece, however, where the disease is very common in dogs and skin lesions are not rare, the infection is due only to the parasite of visceral leishmaniasis. We could not trace by the usual laboratory tests a single case in dogs due to *L. tropica* (BLANC and CAMINOPETROS, 1930; CAMINOPETROS, 1934).

Canine leishmaniasis is found in all the regions of Greece in which human visceral leishmaniasis is known to occur. The people know the relation which exists between human and canine disease. It is very often said that in the same house, or in neighbouring houses, a canine case preceded a human case of the disease.

The clinical picture in dogs, as is well known, is characterized by emaciation, trichoptosis, eczema furfuraceum, ulceration of the skin and the mucous membranes, diarrhoeic motions and sometimes eye symptoms (conjunctivitis, keratitis). We noticed characteristic ulceration at the base of the ear. It must be emphasized that, very often, infected dogs appear to be macroscopically absolutely normal and healthy, and in our mass examinations in the Canea region (MAYER and MALAMOS, 1936, MALAMOS, 1936, 1937) we found 50 per cent. of the infected dogs with this normal appearance.

In canine leishmaniasis the parasite is found in the internal organs: namely the spleen, liver, bone-marrow and intestine. The skin, however, is the tissue which seems to contain the greatest numbers of leishmania in histiocytes, which may also be found in parts of the skin which macroscopically seem to be normal.

As in other Mediterranean countries, canine leishmaniasis is in Greece more common than human kala azar, and it is the endemic form of *L. donovani* infection—sometimes epidemic—which, normally infecting dogs, attacks human beings also. I may mention, for instance, that from examination of dogs the following percentages of infection were established: in Athens CARDAMATIS (1911) found 8·15 per cent.; LÉPINE and BILFINGER (1936) 11–12 per cent.; in Piraeus CARDAMATIS (1911) 7·5 per cent.; in Hydra LIGNOS (1932) 16·6 per cent.; in Canea (Crete) PAPANTONAKIS (1939) 20·5 per cent.; ADLER, THEODOR and WITENBERG (1938) 10 per cent.; MAYER and MALAMOS (1936, 1937) 5·1 per cent.; and in Mani CAMINOPETROS (1934) 16 per cent. During August–October 1935, out of 666 dogs examined in Canea (MAYER and MALAMOS, 1936; MALAMOS, 1936, 1937) and the neighbouring villages, all the infected dogs which we found came from districts of the town and villages where human

kala azar cases were to be traced (Canea ; Hag. Ioannis, Hag. Loukas, Amperia, Dikastiria, Chalepa, and the villages Katsifariana, Mournies, Perivolia). Not a single dog from Splantzia was found infected ; Splantzia, the old Turkish centre of the town of Canea, is the endemic region of oriental sore. Similar observations were published later by ADLER, THEODOR and WITENBERG (1938), and by PAPANTONAKIS (1936, 1939).

It is obvious that if we want to be successful in preventing the spread of human visceral leishmaniasis, we must direct our campaign, first towards the infected dog, the reservoir of the parasite. It was with this object that PAPANTONAKIS (1939), medical inspector of the Canea district, issued an order, published in the official Gazette, 1937, Nr. 79, Vol. B., the text of which is as follows :—

" Each April, the dogs of Canea and its neighbourhood must be presented for examination to the Hygiene Centre. The dogs which are found to be infected with *L. donovani* will be destroyed. Where a case of human visceral leishmaniasis is detected in a village of the Canea district, all the dogs of this village will be destroyed. If the owner of a dog from such a village desires his dog not to be destroyed, he must present it for examination to the Hygiene Centre of Canea, and the local Police authorities will notify him if the dog is found to be healthy and can be kept. The inhabitants of such a village will have the right to acquire other dogs :—

(1) only in the months of January and February of the following year ;
(2) the new dogs must be more than two months old ;
(3) they must come from villages where human kala azar has not been detected."

The war, and enemy occupation, prevented the further application of this order, and so we are not able statistically to evaluate the expected improvement.

Last, but not least, I must mention the mode of transmission of leishmaniasis. This transmission is now proved to take place through the sandfly, and not by the dog tick *Rhipicephalus sanguineus*, as was supposed by some scientists (in Greece, for instance, by BLANC and CAMINOPETROS, 1930). It is to the excellent work of SHORTT in this field that we owe the definite proof of a hypothesis which was put forward some years ago.

Phlebotomus perniciosus is considered to be the vector of human and canine visceral leishmaniasis in most of the Mediterranean countries. The investigations of ADLER and THEODOR (1932) and of ADLER, THEODOR and WITENBERG (1938) and ourselves have proved that for Greece, *Phlebotomus major*, and not *Phlebotomus perniciosus*, must be considered as responsible for the transmission of this disease. *Phlebotomus major*, containing flagellates, were found in houses where human kala azar existed (ADLER, THEODOR and WITENBERG, 1938). The successful infection of *Phlebotomus major* with flagellates was experimentally demonstrated (2–70 per cent.) after feeding them on infected dogs (ADLER, THEODOR and WITENBERG, 1938). In Greece, the main vector of oriental sore, on the other hand, is *P. sergenti* ; and only occasionally is *P. papatasi* involved.

I believe that by this general and short survey of the vectors of leishmaniasis the co-existence of the three forms of the disease can be explained ; we observed these associations particularly in Canea. Thus, oriental sore occurs principally in the old Turkish centre of the town, called Splantzia, in which the majority of the inhabitants are refugees from Asia minor. In this place the streets are very narrow and there is a lack of vegetation. In this area we did not find *P. major* ; 53 per cent. of the collected sandflies were *P. sergenti* and 47 per cent. *P. papatasi*. None of the 136 dogs examined was infected with *L. donovani*.

Plan of Canea showing distribution of human kala azar, canine leishmaniasis, and oriental sore.

On the contrary in the peripheral regions of the town, where the houses are of the bungalow-type, with small gardens and some vegetation, human and canine visceral leishmaniasis are common. Here 49 per cent. of the sandflies examined were *P. major*, 45 per cent. *P. papatasi*, and only 6 per cent. *P. sergenti* (MAYER and MALAMOS, 1936).

Let us hope that by the measures taken against infected dogs, as well as by the improvements in insecticides, we shall be able to eradicate these diseases.

REFERENCES.

ADAMOPOULOS, C. (1926) *Grèce Méd.*, v. 28, 26.
ADLER, S. & THEODOR, O. (1931) *Proc. Roy. Soc.* Ser B., v. 108, 447. [*Trop. Dis. Bull.* 1932, v. 29, 103.]
—— & ——. (1932) *Ibid.*, v. 110, 402. [*Trop. Dis. Bull.* 1932, v. 29, 872.]
—— & ——. (1932) *Nature*, Oct. 1, 507. [*Trop. Dis. Bull.* 1933, v. 30, 318.]
—— —— & WITENBERG, G. (1938) *Proc. Roy. Soc.* Ser. B., v. 125, 491. [*Trop. Dis. Bull.* 1939, v. 36, 443.]
ALEXANDRIDES, K. (1929) *Arch. f. Schiffs- u. Trop.-Hyg.*, v. 33, 542. [*Trop. Dis. Bull.* 1930, v. 27, 90.]
BLANC, G. & CAMINOPETROS, J. (1927) *Ann. Inst. Pasteur*, v. 41, 1002. [*Trop. Dis. Bull.* 1928, v. 25, 73.]
—— & ——. (1928) *Grèce Méd.*, v. 30, 9. [*Trop. Dis. Bull.* 1929, v. 26, 327.]
—— & ——. (1930) *C. R. Acad. Sci.*, v. 191, 800. [*Trop. Dis. Bull.* 1931, v. 28, 153.]
—— & ——. (1930) *Ibid.*, 1162. [*Trop. Dis. Bull.* 1931, v. 28, 640.]
CAMINOPETROS, J. (1934) *C. R. Soc. Biol.*, v. 115, 910. [*Trop. Dis. Bull.* 1934, v. 31, 657.]
——. (1934) *Bull. Soc. Path. Exot.*, v. 27, 443. [*Trop. Dis. Bull.* 1935, v. 32, 82.]
——. (1934) *Ibid.*, 450. [*Trop. Dis. Bull.* 1935, v. 32, 82.]
——. (1934) *Ibid.*, 527.
CARDAMATIS, J. P. (1911) *Cent. f. Bakt.* I. Abt. Orig., v. 60, 511.
——. (1912) *Bull. Soc. Path. Exot.*, v. 5, 489. [*Trop. Dis. Bull.* 1912, v. 1, 5.]
COPANARIS, P. (1935) *Bull. Office Internat. d'Hyg. Pub.*, v. 27, 1570. [*Trop. Dis. Bull.* 1936, v. 33, 18.]
DIWARIS, S. (1914) *Iatriki Proodos*, v. 19, 132. [*Trop. Dis. Bull.* 1914, v. 4, 395.]
DOUCAS, C. (1929) *Bull. Soc. Française Dermat. et Syph.*, No. 5, 469. [*Trop. Dis. Bull.* 1929, v. 26, 751.]
HIGOUMENAKIS, G. K. (1938) *Arch. f. Dermat. u. Syph.*, v. 178, 133. [*Trop. Dis. Bull.* 1939, v. 36, 453.]
JOANNIDÈS, G. S. (1926) *Grèce Méd.*, v. 28, 33. [*Trop. Dis. Bull.* 1927, v. 24, 846.]
KIRIMLIDIS, D. (1938) *Muench. med. Woch.* v. 85, 1143. [*Trop. Dis. Bull.* 1938, v. 35, 859.]

Lignos, A. (1932) *Bull. Soc. Path. Exot.*, v. 25, 1043. [*Trop. Dis. Bull.* 1933, v. 30, 321.]
Lépine, P. & Bilfinger, F. (1936) *Ibid.*, v. 29, 131. [*Trop. Dis. Bull.* 1936, v. 33, 508.]
Malamos, B. (1936) III. Congr. Intern. de Pathol. Comparée, Athens, v. 2.
——. (1937) *Arch. f. Schiffs- u. Trop.-Hyg.*, v. 41, 240. [*Trop. Dis. Bull.* 1937, v. 34, 573.]
——. (1937) *Ergebn. f. inn. Med. u. Kinderheilk.*, v. 52, 1.
Matarangas, G. (1927) *Bull. Office Internat. d'Hyg. Pub.*, v. 19, 1453. [*Trop. Dis. Bull.* 1928, v. 25, 426.]
Mayer, M. & Malamos, B. (1936) *Arch. f. Dermat. u. Syph.* v. 174, 225. [*Trop. Dis. Bull.* 1937, v. 34, 40.]
Pangalos, G. C. (1929) *Grèce Méd.* v. 31, 17. [*Trop. Dis. Bull.* 1930, v. 27, 99.]
Papantonakis, E. (1935) *Ann. Trop. Med. & Parasit.*, v. 29, 191. [*Trop. Dis. Bull.* 1936, v. 33, 17.]
——. (1936) *Bull. Office Internat. d'Hyg. Pub.*, v. 28, 852. [*Trop. Dis. Bull.* 1937, v. 34, 41.]
——. (1936) *Arch. f. Schiffs- u. Trop.-Hyg.*, v. 40, 141. [*Trop. Dis. Bull.* 1936, v. 33, 500.]
——. (1939) *Ibid.*, v. 43, 273. [*Trop. Dis. Bull.* 1939, v. 36, 1028.]
Phinos, V. G. (1932) *Ibid.*, v. 36, 515. [*Trop. Dis. Bull.* 1933, v. 30, 320.]
——. (1932) *Ibid.*, 594. [*Trop. Dis. Bull.* 1933, v. 30, 319.]
Spyropoulos, N. (1928) *Med. Klin.*, v. 24, 1865. [*Trop. Dis. Bull.* 1929, v. 26, 316.]

The following additional references should be consulted :—
Botzaris, A. (1939) *Folia Haematologica*, v. 62, 215. [*Trop. Dis. Bull.* 1940, v. 37, 347.]
Caminopetros, J. (1935) *Bull. Soc. Path. Exot.* v. 28, 44. [*Trop. Dis. Bull.* 1935, v. 32, 674.]
Cardamatis, J. P. (1931) *Ibid.*, v. 24, 287.
Makkas, G. & Papasotiriou. (1917) *Archia Iatrikis.* Athens, No. 18.
Papadakis. (1935) II. Med. Congr. Saloniki, pp. 326–34 ; 335–51.

EXUDATE FROM MILLIPEDES WITH PARTICULAR REFERENCE TO ITS INJURIOUS EFFECTS.

By E. Burtt, Ph.D., D.I.C.

The general conception is that Centipedes (Chilopoda) and Millipedes (Diplopoda) are closely related. This view persists largely because in the old scheme of classification they were placed together as orders in the same class—the Myriapoda. For convenience both continue to be treated under this head in the Zoological Record and in such standard works as the revised edition of Parker and Haswell (1940). However, in modern practice, they are recognized as being so widely divergent zoologically as to merit being regarded as distinct classes of the Arthropoda—having no more connexion with one another than have, for example, the Arachnida and the Insecta (Kükenthal and Krumbach 1926–1927, Patton and Evans 1929). Centipedes are carnivorous, while millipedes are vegetarian feeders. The painful bites which some of the former (*e.g. Scolopendra*) can inflict are well known. In their case, venom produced from a gland in each of the two poison-jaws, is introduced into the victim through a pore near their apices in the act of biting. In certain species the poison glands are too large to be contained in the poison jaw and are situated in the abdominal segments. Many centipedes of the order Geophilomorpha have the chitinous disc of the ventral part of each segment pierced by very fine pores. These are the openings of unicellular glands from which odorant liquids having phosphorescent or venomous properties may be secreted (Phisalix 1922). Patton (1931) refers to *Otostigmus lineatus** as a common pest in Tonkin. During the daytime it hides in cracks and crevices in walls and

* This species is attributed by Patton to the Diplopoda. Nevertheless other authorities (*e.g.* Attems, 1926–1930) place it in the Chilopoda, order Scolopendromorpha.

only comes out at night. It is said to crawl up on to a bed and, owing to its small size, to pass easily through the mesh of a mosquito curtain. As soon as it is touched, it emits a phosphorescent vesicant fluid which is reputed to cause painful blisters. However, since *O. lineatus* Hasse 1887 has a length up to 45 mm. (ATTEMS 1930) and phosphorescence does not appear to be known among the Scolopendromorpha (VERHOEFF 1902–1925, PHISALIX *loc. cit.*, ATTEMS 1926–1930, KOCH 1927), it would appear that the identification was incorrect, and that the creature (along with other species having similar habits) referred to was probably, in fact, a member of the Geophilomorpha.

Millipedes cannot injure man or animals by biting. The general view is that they are harmless creatures (Patton and Evans) which can be handled with impunity. Nonetheless members of the group are recognized as injurious by certain peoples in tropical countries (LOOMIS 1936, 1941) and in some regions natives regard them with dread (BURTT 1938a, MUSGRAVE 1943). Although the Diplopoda are provided with no mechanism with which to inoculate poison, the majority are possessed of the defensive power of exuding repugnatorial fluid from segmentally arranged glands (WHITTICK 1943). The fact that contact with this fluid may cause injury of a serious nature is not widely recognized. Few authenticated instances are known. This opportunity is taken to assemble data on the subject.

Diplopoda are divided into two sub-classes—Pselapognatha and Chilognatha. The former are a small group of inconspicuous, soft-bodied creatures, devoid of repugnatorial glands and so do not concern us. The great majority of millipedes belong to the Chilognatha. These have the chitinous covering of the body strengthened with calcareous matter and repugnatorial glands are usually present. They include such diverse forms as Glomerids (Pill-millipedes), Polydesmids (flat-backed millipedes) and the Juliformia (ATTEMS 1926–1930) —the order to which the few forms known to be injurious belong (" Ordinary " millipedes, of which *Julus terrestris*, popularly known as " wire-worm "*, is a familiar example). A Juliform millipede is to be found figured in most text-books on the subject. These creatures have a hard casing, are long and cylindrical (circular in cross-section) and possess more than 40 segments. When disturbed their habit is to coil up into a flat spiral. Along each side of the body is a continuous row of pores (repugnatorial foramina, WAGA 1839) through which defensive fluid can be extruded. A single pore occurs on each side of each segment from the 5th or 6th back to the last one which bears legs. Tropical forms may attain a length of 300 mm. (VERHOEFF 1926–1928, BURTT 1938) and are often conspicuous objects. Included in the Juliformia are such genera as *Julus*, *Spirobolus*, *Rhinocrichus* and *Spirostreptus*.

In members of the group the secretory mechanism has been described for *Spirobolus cupulifer* Voges by VOGES (1878) (quoted by VERHOEFF) and for *Pachyiulus flavipes* Latz. by ROSSI (1903) and VERHOEFF. Each repugnatorial foramen leads, by a narrow channel, to a multicellular, retort-shaped gland which is embedded and fixed amongst the tissues in the side of the segment concerned. Each segment with foramina thus possesses two glands for secretion of repugnatorial fluid. They possess no contractile elements in their walls, expulsion of the fluid being apparently due entirely to its being under pressure from the surrounding tissues. The channel connecting the glandsac with the foramen is blocked by a stout, grooved, chitinous rod whose distal end plugs the opening. This rod is connected by a muscle to the projecting ventral margin of the preceding segment. When the muscle is not in use the apparatus is closed, but when it contracts, the chitinous rod is pulled inwards and downwards, thus withdrawing the plug from the foramen and also leaving

* Not to be confused with " wire-worm " as applied to larvae of click-beetles (Elateridae).

a channel on its dorsal side along which fluid (under pressure from within) can escape to the exterior.

Secretions from millipedes have long attracted attention on account of their colour and smell. Verhoeff states that the most frequent hues are yellow-brown or brown, but red, lemon-yellow, white, or clear and colourless examples also occur. There are forms in which the exudate appears to be gaseous (Verhoeff). Waga (1839) likened the smell from *Glomeris* to chlorine ; some Lysiopetaloidea smell of excrement or urine (Verhoeff) ; Polydesmids, when stimulated, usually smell of bitter almonds or prussic acid (Phisalix, Verhoeff, Weber 1882, Cope 1883, Wheeler 1890, Burtt 1938a, Turk 1945–1946). According to Harvey (1940) certain Polydesmids have been described as luminous. In Juliformia the secretion has been described as lemon-yellow (Verhoeff, Loomis 1941), yellow (Savy 1823, Cope), yellow-brown or like iodine (Burt, Musgrave). Its smell is pungent. Thus Cope (1883) likened the odour from American species to that of aqua regia. Phisalix (1900) thought the fluid from *Schizophyllum mediterraneum* smelled more like bromine than chlorine, without being identical with either, but subsequently Béhal and Phisalix (1900) stated it was identical with quinone both as to smell and other properties. According to Verhoeff, Vaubel in 1901 remarked that German members of the group produced a chlorine-like or iodine-like smell. Verhoeff states that *Pachyiulus foetidissimus* Muralewicz gives off a penetrating reek of garlic. Turk considered *Cylindroiulus punctatus* smelled of hydrochloric acid. Burtt thought the exudate of certain Tanganyikan species had an odour like nitrogen peroxide gas. The secretion is oily in character (Weber 1882). From *Schizophyllum mediterraneum* it was a light volatile liquid, only slightly soluble in water, but more so in alcohol (Phisalix 1900), the aqueous solution was neutral to litmus and the active principle distilled over readily, apparently unchanged (Béhal and Phisalix). Similar properties were noted by Führt (1903) in the case of German species. It stains the skin yellow, yellow-brown or reddish-brown, in this respect resembling closely the effect of iodine solution (Holl 1826 mentioned by Verhoeff ; Burtt). The stains do not wash off (Phisalix 1900) even after repeated application of soap and water (Verhoeff).

The defensive fluid usually just oozes from the repugnatorial foramina forming droplets along the sides of the body. This was first remarked by Savy (1823), prior to whose observations these foramina were wrongly interpreted as tracheal openings (Phisalix 1922). The last-named author also mentions that in some tropical *Spirobolus* and *Spirostreptus* the venom can be squirted. Verhoeff mentions this also for certain *Pachyiulus*, *Lysiopetalum* and *Appelbeckia*. Of particular interest are observations recorded by Loomis (1936). He found that *Rhinocrichus lethifer* Loomis in Haiti habitually squirted fluid a distance of several inches when disturbed and one specimen projected its venom about 18 inches. On a subsequent occasion in Haiti he records (1941) *Rhinocrichus latespergor* Loomis behaving similarly. A number were released on a cement floor and irritated with a long switch. Several were able to squirt their fluid a distance up to 24 inches, but the maximum achievement was a double salvo from an animal which sent its discharge 28 inches on one side and 33 inches on the other. In all these cases fluid left the body so suddenly and in such fine jets that it could scarcely be seen before it fell on the cement floor in tiny droplets distributed somewhat fan-wise from the body. Squirting of fluid by large millipedes in New Guinea was observed by McNamara (Musgrave). The present writer witnessed similar behaviour by a large Juliform in Tanganyika Territory, but did not record this observation at the time. Three species were frequently seen near Amani. Fluid was extruded when the animals had coiled up after being disturbed. From the two smaller (about 6 inches in length) fluid was only exuded in droplets along the sides, but in the case of the largest

species (10–12 inches in length) it was squirted. Frequently several fine jets were projected simultaneously. The fluid was shot out along an oblique plane (inclined upwards at about 30 degrees) with the horizontal, thus landing in the vicinity around the creature as it lay coiled up on the ground. In all three species, as long as the millipedes had evident fluid to extrude, it remained quiescent when molested, but as soon as its supplies were seemingly getting exhausted it would uncoil and make every effort to escape.

Injurious Effects of the Secretion.—Since millipedes have no means of inoculating their secretion, poisoning effects produced in animals by experimental sub-inoculation will not be considered here. Verhoeff recorded getting a small wound in the finger contaminated with the fluid while collecting *Pachyiulus* and Lysiopetalids. The following night and to a lesser extent the one after, he developed a violently itching nettle-rash on many parts of the arms and legs. He ascribed this trouble to the effect of the millipede poison. Cases are on record where the prussic-acid-like exudate of Polydesmids has proved lethal to the animals which produced it when they were confined in bottles and acted similarly on other small creatures (Phisalix 1922). Apart from these instances records of injurious effects seem to be confined to the Juliformia—particularly to the venom-projecting species.

The fact that the fluid discolours human skin has already been mentioned. It also has a corrosive action (Verhoeff) and the affected skin may desquamate (Phisalix *loc cit.*, Loomis 1936). It may give rise to a tingling sensation (Phisalix *loc. cit.*, Turk). The fluid from *Rhinocrichus lethifer* caused smarting when it came in contact with the moist skin of the back of the hands and lower forearm (Loomis *loc. cit.*). Burtt tested fluid on himself and found that mere contact with the tough skin of the fingers produced no injurious symptoms, but when it was rubbed on the skin of the leg smarting resulted and the skin subsequently became hard and scaly; fumes from this secretion caused marked watering of the eyes. Gravely (1915) mentions that certain of the larger Indian species exude an evil smelling coloured fluid when disturbed. In one species he records "a particularly virulent fluid which not only smells but stains and burns one's hands."

Known injuries of a more serious nature from secretion of Juliformia fall into two categories :—(*a*) caustic action on the skin, (*b*) injury to sight.

(*a*) *Caustic action on the skin.*

The first recorded instance of man suffering injury of a serious nature from a millipede appears to be the experience suffered by Loomis (1936, 1941). In Haiti in 1927, a large coiled-up specimen of *Rhinocrichus lethifer* squirted its defensive fluid into his face and left eye. Pain was immediate, of an intense burning and smarting nature. It persisted for several hours, despite the fact that the affected parts were bathed forthwith in ice-water to remove the secretion. Swelling of the eye-lid and cheek progressed rapidly and soon the eye was closed. It remained in this condition for several hours, after which pain and swelling began to subside. By the following morning pain had ceased but swelling had closed the eye again. The swelling was rapidly reduced by application of cold water. The same was the case the following morning. The day after the attack, the skin of the cheek, forehead and eyelid had turned dark brown and was raised in blisters where the concentration of the fluid had been greatest. The blisters persisted for nearly a week, after which the discoloured skin peeled off without leaving any scars and no further ill effects were experienced.

In 1937 near Amani, Tanganyika Territory, Burtt also suffered injury from the secretion of a squirting-species of Juliform. The case differed from that detailed above chiefly in the fact that contact of the caustic fluid with the skin

was prolonged and there was not the consciousness of immediate pain. A millipede* was picked up and placed in the hip pocket where it was left for about an hour. The creature was felt moving about and slight soreness developed in that region. Soon afterwards, on inspection, it was found that the skin over the corresponding area of about nine square inches was black and inflammation was extending right down the thigh. The pocket had become soaked with exudate and the soaked cloth had been pressed against the skin; no blisters were produced. Four days later all the blackened skin sloughed off, leaving a raw wound. The scar of the injury was still clearly defined more than a year later.

(*b*) *Injury to sight.*

Loomis (1936) remarked that local natives in Haiti were thoroughly familiar with the ability of *Rhinocrichus lethifer* to blind small animals, especially chickens, but he had no evidence that the fluid had any direct lethal action. Blinded chickens were usually killed forthwith by their owners or, if left, died of starvation. In his own case, despite the intense pain, no injury to the eye itself seems to have occurred. Probably instinctive blinking of the eyelid had prevented fluid from entering the eye to any extent.

Musgrave quotes the late C. T. McNamara while in Papua as having written to the Australian Museum that a very large species of millipede, common in the bush there, was held in great dread by the natives. They stated it was able to squirt out a jet-black viscid fluid which would cause blindness if it entered the eye. He personally had not met with a single instance to bear out this rumour; he had often molested the millipedes on purpose and had them shoot out jets of iodine-like fluid into his open palm. However, despite the lack of corroboration of injury to man, McNamara stated he actually did witness his own puppy get fluid squirted into its eye by one of these creatures and the eye concerned went completely blind.

From the above account it will have been noted that whereas in some tropical species venom appears to be habitually squirted, in others from the same area it merely oozes from the repugnatorial foramina, as it does in the majority of European forms. No satisfactory explanation of how the venom comes to be thus projected appears to exist. Verhoeff merely suggests that squirting is an index of a difference in the nervous impulse (influenced by the hot climate) acting on the basic type of mechanism (mentioned above) worked out for some of the European species. The problem seems to want further investigation. Practically nothing is known about the secretory apparatus and exudates in the big exotic species. That some of the latter are very poisonous is indicated by the fact that they yield poison for arrows (Verhoeff). The properties and composition of the venom and the method of its expulsion would undoubtedly repay further study.

References.

Attems, C. G. (1926–30) *Handbuch der Zoologie*. Bd. 4. 1st hälfte. Progoneata, Chilopoda, Insecta 1. Berlin and Leipzig. pp. 223, 317, 342.
——. (1930) Das Tierreich. Myriopoda 2. Scolopendromorpha. 54 Lieferung. Berlin. p. 148.
Béhal & Phisalix, C. (1900) *Bull. Mus. Hist. Nat.* Paris, v. 6, 388.
Burtt, E. (1938) *Nature*, Oct. 29, 796.
——. (1938 *a*) *Tanganyika Notes & Records*, v. 6, 91.
Cope, E. D. (1883) *American Naturalist*, v. 17, 337.
Gravely, F. H. (1915) *Records of the Indian Museum*, Calcutta, v. 11, Pt. 6, 517.
Harvey, E. N. (1940) Living Light. Princeton. p. 65.
Koch, A. (1927) *Zeit. Morp. Okal.* Berlin, v. 8, 241.

*The actual specimen, 12 inches in length, is preserved in the Zoological Museum, the University of Reading, England. Its identification is uncertain but it was regarded as a species of *Spirobolus*.

KÜKENTHAL, W. & KRUMBACH, T. (1926–7) *Handbuch der Zoologie.* Bd. 3. 1st halfte. Tardigrada, Pentastomida, Myzostomida, Arthropoda, Allgem. Crustacea. Berlin and Leipzig. p. 276.
LOOMIS, H. F. (1936) *Bull. Mus. Comp. Zool.* Harvard, v. 80, 1.
——. (1941) *J. Wash. Acad. Sci.*, v. 31, 188.
MUSGRAVE, A. (1943) *Aust. Mus. Mag.* Sidney, v. 8, 132.
PARKER, T. J. & HASWELL, W. A., revised by LOWENSTEIN, O. (1940) A Text Book of Zoology. 6th edition, Vol. 1, p. 459.
PATTON, W. S. (1931) Insects, Ticks, Mites and Venomous Animals of Medical and Veterinary Importance. Part 2. Public Health. Liverpool. p. 690.
—— & EVANS, A. M. (1929) Insects, Ticks, Mites and Venomous Animals of Medical and Veterinary Importance. Part 1. Medical. Liverpool. pp. 16, 694.
PHISALIX, C. (1900) *Bull. Mus. Hist. Nat.* Paris, v. 6, 385.
PHISALIX, M. (1922) Animaux venimeux et venins. Vol. 1. Paris. p. 177.
ROSSI, G. (1903) *Ztschr. wiss. Zool.* Leipzig. v. 74, 64.
SAVY, P. (1823) *Isis*, v. 12–13, 214.
TURK, F. A. (1945–6) *Northwestern Naturalist*, v. 20, 143.
VERHOEFF, K. W. (1902–25) (Section on Centipedes in Bronns Tier-Reichs). Bronns, H. G. (1925). *Klassen und Ordungen des Tier-Reichs.* Bd. 5. 2. Abteilung Gliederfüssler: Arthropoda Klassa Chilopoda. Leipzig. p. 310.
——. (1926–28, 1928 32). (Millipede section in Bronns Tier-Reichs). Bronns, H. G. *Klassen und Ordnungen des Tier-Reichs.* Bd. 5. 2. Abteilung Gliederfüssler: Arthropoda, Klassa Diplopoda. Leipzig. 1st & 2nd Parts, pp. 1–4, 26–36; 60, 122–4, 1016–29, etc.
VON FÜHRT, O. (1903) *Vergleich Chem. Physiol. d. niederen Tiere.* Jena. p. 332 (über myriap).
WAGA, A. F. (1839) *Rev. zool. par la Soc. Cuvierienne.* v. 2, 76.
WEBER, M. (1882) *Arch. f. mikr. Anat.*, v. 21, 468.
WHEELER, W. M. (1890) *Psyche.* v. 5, 442.
WHITTICK, R. J. (1943) Arachnida, Penastomida, Myriapoda in J. Smart's Handbook, Identification of Insects of Medical Importance. Brit. Museum. London. p. 255.

SUMMARY OF RECENT ABSTRACTS.*

I. CHOLERA.

Epidemiology: Aetiology.

STOWMAN (p. 128) has written an account of the distribution of cholera during the present century; this does not lend itself to abstraction, and should be consulted in the original.

SEAL (p. 217) points out that the problem of the endemicity of cholera is still not understood. The Bengal Cholera Field Enquiry found that the vibrio could not be isolated from the stools of the general population, or from water in the endemic area, except in direct relation to the cholera case, but the present author states that we still do not know where and how the cholera vibrio exists before a case occurs in an endemic area.

PANJA and GHOSH (p. 218) show that curdled milk (a common food in India, *p*H 4·2 to 4·7) is lethal to *V. cholerae* in a few minutes, but that for typhoid and dysentery bacilli its action is not so rapid. Hydrochloric acid is also quickly lethal to *V. cholerae* at *p*H 4·4, as is lime juice at the same *p*H value. The other organisms are more resistant. YACOB and CHAUDHRI (p. 649) have shown that aerated drinks (soda water and lemonade) infected with cholera vibrios will in time be rendered harmless by their own action. It is probable that water containing the vibrios, if converted into ice and served in drinks, may also not prove harmful.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1946, v. 43. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

Soman and Nail (p. 439), during epidemics of cholera in Bombay in 1943 and 1945, found that 161 of 164 strains of the vibrio were of the Ogawa subtype, the remaining 3 being Inaba.

Binson (p. 217) discusses the various tests used for the classification of vibrios, and mentions in particular the Gipsen test, which serves to differentiate the El Tor from the cholera vibrio. This test depends on the fact that the El Tor vibrio, after having been heated, in suspension, at 56–57°C. for 3 hours, is still completely agglutinable, whereas the cholera vibrio is only partially, or not at all, agglutinable after the same treatment. This test should be most valuable to the epidemiologist, who must use with discernment his power to detain travellers.

Panja (p. 218) has obtained rough colonies of *V. cholerae* by growing smooth strains on agar plates containing 1:5,000 atebrin.

Blass (p. 742) has studied the consumption of glucose by cholera vibrios; for details the original should be consulted.

Grabar and Gallut (p. 129) have investigated further the properties of that constituent of the cholera toxin which produces hypothermia. It is probably not a protein, and has no antigenic power; it is a relatively small molecule.

Clinical Findings: Treatment.

Markowitz (p. 741) gives an account of cholera as he saw it in a jungle camp for prisoners of war in Thailand; of 134 cases, 53 were fatal. Treatment with hypertonic saline (2 per cent.) seemed to be more effective than with normal saline. The terrible conditions of these camps are described. de Wardener (p. 742) gives a similar account of an epidemic of cholera in prisoners of war working on the notorious Burma-Thailand railway; the fatality rate was 57·8 per cent. In a Dutch camp the incidence was trifling, and this was probably due to the protective inoculations of vaccine which the Dutch had received.

Yacob and Chaudhri (p. 129) note that agglutinins are present in cholera by the 6th day, but the titre is not very high. It is not known how long they persist, but such knowledge might be useful to the epidemiologist making retrospective diagnoses. The authors investigated this point, and found that the agglutinins may persist up to 3½ months, possibly more.

Chatterjee (p. 555) discusses the phenol content and reserve alkalinity of the blood in cholera. The former is raised, even apart from the increased concentration which would occur as the blood becomes more concentrated. The reserve alkalinity of the blood is decreased, and this effect persists longer than the increase in blood phenol. Clinical improvement runs parallel to improvement in the chemical composition of the blood.

Lefrou *et al.* (p. 554) describe the disease known as cholerine in the French Sudan. It is usually mild, but the symptoms resemble those of cholera; it is apparently related to a vibrio, the characters of which are described.

In the Report of the Indian Research Fund Association for 1943 (p. 129) it is shown that in a series of cholera patients treated with sulphaguanidine (20 gm. in 24 hours) the case-mortality rate was 1·72 per cent., whereas in a comparable series of controls it was 6·32 per cent. It is also shown that "reactions following intravenous injections of saline solutions are due to pyrogen (a bacterial product), an oxidizable matter and higher or lower hydrogen ion concentration of the solution." "Pyrogen-free water can be prepared by treating water with acid potassium permanganate," by a technique which is described, and by distillation; the optimum *p*H is 7·1. [See also Campbell and Cherkin, below.] In the Report of the same association for 1944 (p. 130) it is reported that in an epidemic of cholera, 79 per cent. of a series of patients treated with sulphaguanidine recovered, whereas only 25 per cent. of a control

series did so. Tests of sulphasuxidine were disappointing. GUPTA *et al.* (p. 130) treated 263 cholera patients with sulphaguanidine, and 262 alternate-case controls without that drug. Salines were used as necessary in each series. Of the drug-treated patients 3 died, and of the controls 13. In the sulphaguanidine group there were 86 patients with suppression of urine ; of these, 72 passed urine within 24 hours of taking the drug. In the controls there were 72 cases of suppression, but only 23 passed urine in 24 hours. The dosage of sulphaguanidine reached 20 gm. in 24 hours. In the *United States Naval Medical Bulletin* (p. 440) there is an evaluation of chemotherapy (sulphaguanidine, sulphadiazine or penicillin) in the treatment of cholera, cases treated by these means and also by salines as necessary, being compared with those treated by salines and supportive measures only. There were no deaths in 35 cases in which plasma was administered as well as chemotherapy, 1·1 per cent. of 274 patients on chemotherapy died, and 38·3 per cent. of 37 controls on salines and supportive measures only. There can, therefore, be little doubt of the value of chemotherapy. For sulphaguanidine, 72 gm. were given in 6 days ; for sulphadiazine, 30 gm. in 3 days.

CAMPBELL and CHERKIN (p. 555) note that the true chemical nature of pyrogens is not known, but that they exhibit the properties of polysaccharides. The authors found that pyrogenic solutions can be rendered non-pyrogenic by heating with potassium permanganate or hydrogen peroxide ; the change is not due to alteration of *p*H.

GREIG (p. 927) has contributed an interesting historical account of the use of intravenous saline injections in cholera by Dr. Latta of Leith in the early 19th Century.

Vaccination.

In the Report of the Indian Research Fund Association for 1943 (p. 131), statistical evidence is produced that the injection of cholera vaccine is undoubtedly very effective in protecting against infection. Protection is maximal on and after the tenth day after inoculation, and it is calculated that uninoculated persons are ten times as liable to infection as inoculated persons. The statistical basis of this investigation appears to be quite valid ; the inoculated persons (392,115) were given a single dose of Inaba-Ogawa vaccine. In the Report of the same association for 1944 (p. 131) the account of the investigation referred to above is carried further, and the results reported are confirmed. The number of protected persons numbered 709,977, and the incidence of cholera in them was 1·57 per 1,000, against 16·2 in a larger unprotected population. It was found that there was considerable protection in persons inoculated some time before the second outbreak in villages affected twice, and it is calculated that immunity may persist in an inoculated population for 10, or even 12 months.

FELSENFELD and YOUNG (p. 332) have found that the best cholera vaccine is produced by using formol-killed or heat-killed Inaba strain combined with formolized filtrate of Inaba or El Tor strains (the El Tor strain being finally selected). This vaccine, and others against bacillary dysentery, retained immunizing power much longer if desiccated in a vacuum. Formolized organisms, combined with formolized filtrate, give rise to the strongest and most lasting antibody production. *Charles Wilcocks.*

MALARIA.

PUTNAM, P. & HACKETT, L. W. **An Appraisal of the Malaria Endemic in Protected and Comparison Areas of Sardinia in the Years 1925–1934.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, Mar., v. 5, No. 1, 13–37, 9 figs.

General antilarval measures were begun in Portotorres, a town with 6,000 inhabitants on the north-west coast of Sardinia, in 1925. The object was to determine what a limited programme could accomplish in a highly malarious community. The parasite rate then was 34 per cent. and the spleen rate 47 per cent. among children from 1 to 12 years of age. The carriers were *A. labranchiae labranchiae* and *A. sacharovi*, which was rare ; *A. algeriensis* was also found. Three other Sardinian towns were observed as comparison areas. The objects of the present paper are to compare the trend of the malaria, endemic in these towns, during a ten-year period, and to demonstrate analytical methods best suited to bring out time trends, area differences and interrelationships of the indices employed. These indices were *Anopheles* density, malaria incidence, infant infection rates, parasite and spleen rates, average spleen and average enlarged spleen rates. The various statistical methods employed are described.

Anopheles density and malaria prevalence in Portotorres declined sharply from 1925 to 1929. In the other towns there was a decline in endemicity from 1929 to 1934, but the spleen and parasite rates and average spleens remained significantly lower in Portotorres. In Portotorres there was an interval of seven weeks between the summer rise of anopheline density and the consequent rise in malaria incidence. *Norman White.*

HERNBERG, C. A. Studier över malaria i Finland åren 1943–1945. [**Malaria in Finland in 1943–1945.**] *Nordisk Med.* 1946, Aug. 30, v. 31, No. 35, 1961–2. Discussion 1962 [VON BONSDORFF, B ; HAGELSTAM, L.]

The incubation period of malaria is accepted to be 10 to 14 days, but in the opinion of some it may be prolonged up to one year, and observations made by the author lend support to this view. In 1944 there was an epidemic of malaria amongst troops in Karelia, amounting to 2,000 cases. Over the same period there were practically no cases of malaria in the main part of Finland. In 1945 a thousand cases of malaria occurred in the country, and the epidemic showed the following features :—(1) most patients were of military age ; (2) cases were scattered over the whole country ; (3) cases occurred in the far north, where the temperature was too low for transmission by mosquitoes to be possible ; (4) in half the cases infection must have occurred before the middle of April if the patients had been infected in the same year ; (5) infection from hibernated mosquitoes was impossible as most localities had been free of malaria in the previous year.

The author concludes that infection must have occurred in the previous year, with an incubation period of one year in one-third of the cases. A follow-up revealed that nearly all had served in Karelia in 1944.

Infectivity is perhaps low towards the end of the summer, so that the parasites remain quiescent in the reticulo-endothelial system. A long incubation period might, on these grounds, be expected to be more common in the North, with its short summers, than in Central Europe, and to be entirely absent in the tropics. *D. J. Bauer.*

RAO, B. A. **Malaria in the Irwin Canal Area, Mysore State. Part I.** *J. Malaria Inst. of India.* 1945, Dec., v. 6, No. 2, 101–8, 3 maps.

—— & NASSIRUDDIN, M. **Malaria in the Irwin Canal Area, Mysore State. Part II.** *Ibid.* 109–28, 3 charts.

The Irwin Canal came into operation in January 1932. A dam across the Cauvery River, 12 miles north of Mysore, formed a reservoir from which the canal takes water some 24 miles, north-easterly, and then traverses a tunnel 2 miles long through the Karighatta-Hulikere range of hills, to irrigate five valleys, which together cover some 400 square miles. The gently undulating irrigated land is from 2,100 to 2,300 feet above sea level and drains into the Shimsha River in which water flowed for only a few months of the year, during and after the monsoon. There are 505 villages in the irrigated area with a total population of about 200,000. The area was generally healthy with only a few malaria foci of low endemicity.

Irrigation is perennial, and a triennial rotation of crops was planned, sugar-cane, paddy and dry crops. Within 3 years the land became saturated with water; the subsoil water rose from 20–40 feet below ground to practically ground level. The overcharged tanks produced a vigorous growth of surface vegetation. The dry lands came under wet cultivation and there was but little pasturage for sheep or cattle. An enormous snail population developed in the tanks and resulting fluke disease of sheep and cattle caused an alarming mortality. An epidemic of malaria was followed by hyperendemic conditions. By 1933 the spleen rates of 25 villages which had been 0–10 per cent. before irrigation had risen to 50–90 per cent.

A. culicifacies is the only anopheline that has been found infected. Malaria transmission is most active from March to June and from October to December. *A. fluviatilis* is suspected of being a carrier also.

An attempt to control malaria in ten villages by the systematic use of paris green is described, and the results of five years work are recorded. Control was effective during the first four years, but with the subsequent development of paddy cultivation within the two-furlong zones surrounding the villages, the malaria prevalence in 1940 had once more become very severe.

Norman White.

WOLFF, A. E. **Malaria in Surinam.** *Bol. Oficina Sanitaria Panamericana.* 1946, Apr., v. 25, No. 4, 335–8, 1 map.

BELLERIVE, A. & DAMBREVILLE, C. El problema de la malaria en Haiti. [**The Malaria Problem in Haiti.**] *Tijeretazos sobre Malaria.* Venezuela. 1946, Mar., v. 10, No. 1, 2–3.

This is an English translation of the author's summary :—

Malaria presents an important sanitary problem in the Republic of Haiti. Some 10,000 to 73,000 cases are reported annually with 100 to 700 deaths. The disease has been present in the country since time immemorial and has had a profoundly adverse effect on its economic and social life.

A Commission from the International Health Division of the Rockefeller Foundation examined 31,285 children and found spleen rates of 18·4 per cent. and parasite rates of 46·3 per cent. In 78 per cent. of the children with enlarged spleens, and in 32 per cent. of those with normal spleens, malaria parasites were found in the peripheral blood.

Following the first efforts in sanitary engineering in Petit Goave by the Section of Malaria Control, the infection rate fell in two years from 86·1 per cent.

to 20·7 per cent. This body was assisted by the Institute of Inter-American Affairs, which enabled the work to be extended.

H. J. O'D. Burke-Gaffney.

DEANE, Helen W. **Studies on Malaria Parasites. II. The Staining of Two Primate Parasites by the Feulgen Technique.** *J. Cellular & Comp. Physiol.* 1945, Dec., v. 26, No. 3, 139–44, 1 fig. & 1 coloured pl. [13 refs.]

As some observers have failed to stain the chromatin of malarial parasites by the Feulgen technique, it has been suggested that the chromatin of these parasites differs from that of other cell nuclei in not containing desoxyribonucleic acid, which is the constituent responsible for successful staining. After a number of trials, with not very satisfactory results, it occurred to the authors that the haematin of the pigment, being an oxidative catalyst, might interfere with the staining by oxidizing the desoxyribose which is produced by the hydrolysing part of the technique. Accordingly the pigment of the parasites in the fixed films was removed by alkaline alcohol (80 per cent. alcohol, 96 parts; 1 per cent. aqueous KOH, 4 parts). It was found that after the removal of the pigment the nuclear material stained well. For routine staining, thin wet or dry films are fixed in Duboscq-Brasil fixative (80 per cent. alcohol 150 cc.; formalin 60 cc.; glacial acetic acid 15 cc.; picric acid 1 gramme) for ½ to 2 hours. The slide is thoroughly washed in water and placed in the alkaline alcohol for 15 minutes. After a thorough washing in water it is submitted to the Feulgen technique. The chromatin in all stages of *P. vivax* and *P. knowlesi* stains well. It is most intense in the merozoites, less so in the trophozoites and schizonts and faint in the gametocytes. It is evident that the chromatin of the malarial parasites, like that of other cells, does contain desoxyribonucleic acid. The appearance of various stages of development of the two parasites is shown in a coloured plate and photomicrographs.

C. M. Wenyon.

FERREBEE, J. W. & GEIMAN, Q. M. **Studies on Malarial Parasites. III. A Procedure for preparing Concentrates of** *Plasmodium vivax*. *J. Infect. Dis.* 1946, May–June, v. 78, No. 3, 173–9, 2 figs. & 1 pl.

In this paper is described a method for separating erythrocytes infected with *P. vivax* from uninfected erythrocytes. The method consists of centrifuging together in a centrifuge tube equal volumes of heparinized infected blood and albumin solution of specific gravity 1071. The normal cells tend to fall to the bottom of the tube, while the infected cells remain suspended in the albumin solution between the layer of plasma and the deposited normal cells.

C. M. Wenyon.

FERREBEE, J. W., GIBSON, J. G. & PEACOCK, W. C. **Studies on Malarial Parasites. IV. Some Observations regarding the Age of the Erythrocyte invaded by** *Plasmodium vivax*. *J. Infect. Dis.* 1946, May–June, v. 78, No. 3, 180–82, 1 fig. [15 refs.]

When radio-active iron is administered intravenously it is incorporated in the haemoglobin molecule within 24 hours. This occurs only in the early stages of development of the erythrocytes, so that the radioactivity of a sample of blood is dependent upon the presence of young erythrocytes formed subsequently to the administration of the iron. In the case of the blood of a patient who had been infected with *P. vivax* and then given an injection of radio-active iron it was found that the radioactivity of the whole blood was considerably less than that of concentrates of infected cells. The inference is that the increase in

radioactivity of the concentrate is due to the fact that the parasite invades by preference the young blood cells on which the radioactivity of the blood depends. *C. M. Wenyon.*

BLACK, R. H. **The Behaviour of New Guinea Strains of *Plasmodium falciparum* and *Plasmodium vivax* when cultivated in vitro.** *Med. J. Australia.* 1946, July 27, v. 2, No. 4, 109–11. [12 refs.]

This is a fuller account of the work described in an earlier note [this *Bulletin*, 1946, v. 43, 816]. It is noted that in the method of culture, in which infected red blood corpuscles are added to serum in the flat-bottomed tube, this serum is an efficient medium, whether taken from the patient suffering from malaria or from another individual not suffering from malaria. In the case of *P. falciparum*, the growth from ring to mature schizont occupied slightly more than 48 hours. At the end of about 12 hours, parasites with irregular outline and some scattered pigment were seen. With further growth the parasites became oval or rounded in outline with compact pigment and undivided chromatin. This stage is referred to as the pre-schizont. Next there is an increase in the chromatin, which becomes scattered through the cytoplasm as a filigree with here and there concentrations giving a beaded effect. This early schizont was rapidly changed to one in which the chromatin became condensed into discrete chromatin segments. Finally the cytoplasm condensed around the nuclei to form merozoites, the pigment forming a single oval compact mass. When the schizont ruptured, the liberated merozoites invaded other red cells, as many as eight being seen in a single one. These merozoites did not develop as readily as the first generation. In the case of *P. vivax*, similar results were obtained, the growth period occupying 48 hours. There were two differences. Firstly there was not the distributed chromatin stage as seen in *P. falciparum*. The single chromatin mass divided into two and these again divided and so on till the requisite number of nuclei were present for merozoite formation. After rupture of the mature schizonts, the liberated merozoites did not enter other red blood corpuscles. It is suggested that as the merozoites of *P. vivax* prefer young cells this may account for their failure to enter the older red cells in the culture tube. Schüffner's and Maurer's dots were seen, but gametocytes were not found. The adhesiveness of cells infected with *P. falciparum* is shown by their tendency to clump and to adhere to any leucocytes which may be present. The failure of the second generation to grow properly raises the question of the nutritional requirements of parasites in culture, an understanding of which might lead to an explanation of the mode of action of anti-malarial drugs.
C. M. Wenyon.

SHUTE, P. G. **The Maintenance of a Strain of *Plasmodium vivax* through Man and Mosquito over a Period of 21 Years.** *Monthly Bull. Ministry of Health & Emergency Pub. Health Lab. Service (directed by Med. Res. Council).* 1946, May, v. 5, 110–12, 1 chart.

An account is given of the strains of malaria parasites which have been maintained at the Malaria Laboratory at the Horton Mental Hospital during the past 22 years. A particular strain of *Plasmodium vivax*, known as the Madagascar strain, as it was taken from a member of the crew of a ship which had just completed a voyage from Madagascar to London, has been maintained uninterrupted, through many hundreds of passages in man and mosquito, over a period of 21 years. At one time it was thought that this was a particularly virulent strain, but it seems that the severity of the attacks produced is due to the careful selection of heavy gametocyte carriers for infecting mosquitoes,

many of which develop over 1,000 oöcysts. At the start the mosquitoes (*Anopheles maculipennis*) were taken wild from animal houses, but after 1933 a strain was raised and maintained in the laboratory from eggs laid by a single female. Among other strains of malaria parasite, a Rumanian strain of *P. falciparum* was maintained over a period of 13 years and one of *P. ovale* for 3 years. *C. M. Wenyon.*

ETHERINGTON, D. & SELLICK, G. **Notes on the Bionomics of *Anopheles sacharovi* in Persia and Iraq.** *Bull. Entom. Res.* 1946, Sept., v. 37, Pt. 2, 191–5, 2 figs.

This paper records some disconnected observations on *Anopheles sacharovi* made in Persia and Iraq during the last months of 1943 and the early part of 1944. This anopheline was usually obtained at places between 500 and 5,000 feet above sea level, but at Shatt-el-Arab it was found at sea level.

At the onset of hibernation *A. sacharovi* seemed to enter houses and stables more frequently; in northern Iraq during August and September it was caught in small numbers in sprayed houses and stables, but in greater numbers in October; the first specimen with fat-body was taken on the 1st October. Between then and 26th October only twenty females out of 343 possessed ovaries beyond stage II. In three visits during the winter to uncontrolled villages on the Persia-Iraq border, the authors obtained adult *A. sacharovi* in increasing numbers; the sporozoite rate was 0·41 per cent. (2 in 486 mosquitoes dissected).

In north-east Iraq, where winter temperatures are low, eggs with well developed floats were obtained in February 1944; but the floats on eggs collected at the same time from the warmer Shatt-el-Arab region were less developed.

In Iraq and Persia, autumn spleen rates of between 60 and 100 per cent. were usually obtained in villages where *A. sacharovi* was found; but in one area south-west of Teheran spleen rates in July and August were only 20 to 28 per cent., though *A. superpictus* also occurred there; much higher rates were recorded at the same altitude 100 miles further north, though only *A. superpictus* and *A. maculipennis* var. *typicus* were present. *H. S. Leeson.*

RAJINDAR PAL. **On the Bionomics of *Anopheles culicifacies* Giles. Part III. The Behaviour of Adults. Part IV. Hypothesis of the Races of *A. culicifacies*.** *J. Malaria Inst. of India.* 1945, Dec., v. 6, No. 2, 217–38, 9 charts; 239–41, 1 fig. [34 refs.]

Routine collections of *A. culicifacies* were made from specially selected catching stations—human dwellings, animal houses and combined dwellings—in Delhi from 1939 to 1943 by the Malaria Institute of India. Routine larval collections were also made. They show that the species is prevalent throughout the year. The first rise in prevalence, in April, corresponds with a gradual rise of atmospheric temperature. A decrease in May and June, the hottest months of the year, coincides with the drying-up of breeding places. The break of the monsoon in July is followed by increased prevalence. Both larvae and adults are most numerous in September, when humidity is very high. In October and November prevalence and temperature show a downward trend but there is no reduction in breeding places. December to February inclusive are the coldest months, and the prevalence of *A. culicifacies*, larvae and adults, is low. The density varies markedly from year to year. The density per man-hour was 3·4 during normal years and 25 during an epidemic of malaria. A density

below 5·0 per man-hour is claimed to be incompatible with malaria transmission. Temperatures from 25 to 30°C., with relative humidity from 60 to 80 per cent., are the most favourable conditions for the longevity and activity of this species. There was no evidence of hibernation or aestivation of adults. The most favoured daytime resting places are in dark houses and cattle sheds. *A. culicifacies* is not an habitual feeder on man. During a malaria epidemic, precipitin tests showed that 10·7 per cent. had fed on man. The maxillary index was 13·0 in both epidemic and non-epidemic years. Biting activity decreases after midnight. After oviposition in summer, *A. culicifacies* may return for a second blood feed the same night. This species does not ordinarily fly more than half a mile from its breeding place.

Intensive morphological studies of *A. culicifacies* from parts of India where it does, and where it does not, transmit malaria failed to reveal any difference indicative of the existence of different races. *Norman White.*

GARTRELL, F. E. & ORGAIN, H. **Notes on the Prolific Production and Dispersion of *Anopheles quadrimaculatus* from Impounded Water Breeding Places.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, Mar., v. 5, No. 1, 79–84, 1 map.

The partial filling of the Kentucky Reservoir on the lower Tennessee River during the late summer of 1944 resulted in prolific breeding of *A. quadrimaculatus*. An investigation was made to determine the distance to which mass dispersion of this mosquito was occurring. The Cane Creek area was selected. Cane Creek is a clear, rapidly flowing stream with gravel bed, very few pools, and very little vegetation. Prior to impoundage of the Tennessee, anophelines were hard to find in this valley. In October 1944, counts of 105 and 195 female *A. quadrimaculatus* were recorded in catching stations 2·8 and 2·3 miles from the reservoir. A maximum count of 1,500 was made at a distance of approximately one mile from the breeding area. The long flights may have been "prehibernation flights". It is possible that the distant dispersions were the result of one or more secondary flights after an initial blood meal.

Norman White.

AMERICAN J. HYG. MONOGRAPHIC SERIES, No. 18, 1946, Feb., pp. vi+50, 20 pls. [32 refs.] **Studies on Brazilian Anophelines from the Northeast and Amazon Regions. I. An Illustrated Key by Adult Female Characteristics for the Identification of Thirty-Five Species of Anophelini, with Notes on the Malaria Vectors (Diptera Culicidae)** [DEANE, L. M., CAUSEY, O. R.; & DEANE, M. P.]. **II. An Illustrated Key by Male Genitalic Characteristics for the Identification of Thirty-Four Species of Anophelini, with a Note on Dissection Technique** [CAUSEY, O. R., DEANE, L. M. & DEANE, M. P.]. **III. An Illustrated Key by Larval Characteristics for the Identification of Thirty-Two Species of Anophelini, with Descriptions of Two Larvae** [DEANE, M. P., CAUSEY, O. R. & DEANE, L. M.]. Baltimore, Md. The Johns Hopkins Press.

These keys to females, male genitalia and larvae of anophelines are based on studies made in the north-east and Amazon regions of Brazil since 1939. The authors' illustrated key to the eggs of thirty species of Brazilian anophelines [this *Bulletin*, 1944, v. 41, 644] is not included in this volume.

The key to female anophelines presented in the first paper is illustrated by some sixty-three drawings of distinguishing morphological characters and is preceded by some remarks on the important malaria vectors, *A. darlingi*, *A. aquasalis*, on two vectors of secondary importance, *A. albitarsis*, *A. pessoai*, and on the introduced vector, *A. gambiae*.

Before the eradication of *A. gambiae* was accomplished, experiments showed that, owing to its domestic habits, preference for human blood and susceptibility to *Plasmodium*, this species was the most dangerous vector. The most efficient indigenous vector is *A. darlingi*, which even when present in small numbers only is able to maintain malaria transmission ; *A. aquasalis*, on the other hand, becomes important only when it is very numerous.

Prior to 1926 many infected specimens identified as *A. albitarsis* were in reality *A. darlingi* ; these species are now easily distinguished and *A. albitarsis* is regarded as of secondary importance. Studies on the morphology and bionomics of *A. albitarsis* indicate that there may be an " *albitarsis* complex " composed of a number of species. *A. pessoai* may become a malaria vector in certain circumstances but is only of local importance.

One table sets out the distinguishing characters of eleven species of the " *tarsimaculatus* complex", and another lists the geographical distribution of the thirty-five species.

In the second paper there is a description of the general morphology of the genitalia of male anophelines, illustrated by schematic drawings, and an account is given of the technique employed in dissection and microscopical examination of the parts. The key is illustrated by photomicrographs of each species

The third paper contains descriptions of the larvae of *Anopheles* (*Nyssorhynchus*) *galvãoi* and *Anopheles* (*Anopheles*) *shannoni*. Besides the key to the larvae which is illustrated by some 90 line drawings, a table is given repeating the geographical distribution, but including some notes on the more usual breeding places. *H. S. Leeson.*

Penfound, W. T., Hall, T. F. & Hess, A. D. **The Spring Phenology of Plants in and around the Reservoirs in North Alabama with particular reference to Malaria Control.** Reprinted from *Ecology*. 1945, Oct., v. 26, No. 4, 332–52, 4 figs. [14 refs.]

Since it has been shown that the extent to which plant organs intersect the water line influences the breeding of anopheline mosquitoes ; that the population density of anopheline larvae is correlated with the intersection value (length of intersection line per unit area) ; and as *Anopheles quadrimaculatus* breeds almost entirely in aquatic, and semi-aquatic, vegetation and flotage, it follows that one method of attack against this mosquito is to remove or control such vegetation.

In 1937 the authors began a study of this subject in reservoirs in the Alabama section of the Tennessee Valley. In this paper they record observations made since that time but chiefly during the years 1941 to 1944 inclusive. They are concerned particularly with the late winter and spring seasons because of the relation of plant phenology at that time with the breeding season of anophelines. They have summarized their observations on fifty-three species of herbaceous plants and forty-nine woody plants, in two tables indicating times of sprouting, full foliage, flowering and fruiting between February and June.

The phenology of these plants is discussed in some detail, taking them singly or in groups according to habit. Herbaceous plants for example are dealt with in three groups, terrestrial, wetland and aquatic and the aquatic plants are further sub-divided into emergent, floating and submerged. Methods of water management suitable for the control of each type of plant involves either maintaining a constant water level for some or fluctuating water levels for others. In the case of the latter, progression, cyclical fluctuation or recession have been studied and may necessitate complete submergence of the plant at a particular period of its development, or dewatering, or cutting with subsequent flooding,

or cutting combined with dewatering. One plant, the alligator weed (*Alternanthera philoxeroides*) has proved particularly obnoxious because of its habit of producing a floating mat which prevents larval control by water level fluctuation. Best results were obtained by spraying it with larvicidal oil.

So far as the phenology of most plants is related to the breeding of anopheline mosquitoes, the important aspect is the production of leaves near or on the water surface, and this can be delayed or prevented by the proper manipulation of water levels; a minimum of recession is found to be the most desirable as it restricts the band of vegetation available for the breeding of *Anopheles quadrimaculatus*.

Readily recognizable indications of the commencement of the anopheline breeding season are the appearance of the first leaves of the lotus (*Nelumbo pentapetala*) the flowering of the cow-lily (*Nuphar advena*) and the flowering of the black willow (*Salix nigra*), which events usually occur two weeks before the initial appearance of larvae of *Anopheles quadrimaculatus*. *H. S. Leeson.*

Brooke, M. M. & Proske, H. O. **Precipitin Test for determining Natural Insect Predators of Immature Mosquitoes.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, Mar., v. 5, No. 1, 45–56.

Many predatory insects suck the fleshy internal structures of mosquito larvae, and discard the chitinous exoskeleton; it is not possible by microscopic examination of their stomach contents to determine their natural food selections. Experiments were therefore made to determine whether a precipitin test might be able to demonstrate the presence of anopheline larvae ingested by aquatic insect predators.

An antiserum was produced by intraperitoneal inoculation of a rabbit with macerated pupae of *A. quadrimaculatus*. This serum reacted with larval, pupal, and adult stages of both anopheline and culicine mosquitoes. Six species of aquatic insect predators that had been starved overnight gave no reaction with the antiserum—*Ranatra fusca* adult, a Hydrophilid larva, a Damsel Fly nymph, a May Fly nymph, *Anax junius* nymph and a Tabanid larva. Two others, *Belostoma sp.* nymph and *Cybister sp.* larva, gave a slight reaction. Except in one instance the precipitin test was able to detect that predators had recently fed upon immature mosquitoes. The one failure occurred when a Hydrophilid had eaten only a small portion of one larva. The experiments show that a precipitin test might be of value in the study of natural enemies of the vectors of malaria and other diseases. *Norman White.*

Birnbaum, D., Goldblum, N. & Kligler, I. J. **Further Observations on the Enhanced Fragility of Red Cells in Malaria Patients.** *Acta Med. Orientalia* (*Palestine & Near East Med. J.*). 1946, June, v. 5, No. 6, 177–84. [11 refs.]

In a previous paper [this *Bulletin*, 1941, v. 38, 562] the authors reported that red cells from malaria patients laked more easily in bile solution than did cells from normal subjects. Quinine enhanced this lytic effect. In the present paper they state that quinine administered *per os* for a week to normal subjects does not influence either the rate of lysis of red cells or the reticulocyte count. The enhanced sensitivity of cells from malarial patients persists for 8 weeks after the attack. Quinine, atebrin and plasmoquine all accelerate haemolysis in the presence of bile. "A particularly remarkable enhancing effect is exerted by atabrine. This drug, itself non-haemolytic in vitro even in a high concentration, hastens lysis in a dilution of 1: 200,000 in combination with bile." The authors suggest that there is thus "need for caution in the use of atabrine as a remedy of Black Water Fever."

The stimulating effects of quinine and atebrin were not due to *p*H changes, although alkali had an inhibiting effect on the lysis. Normal and malarial sera exerted equal inhibitory effects on the haemolytic system. The authors consider that in malaria it is probably the red cell itself which is chiefly affected.

[The synergistic effect of atebrin seen in these experiments is interesting in the light of similar effects observed in other lytic systems by ZYLMANN (this *Bulletin*, 1946, v. 43, 405)]. *B. G. Maegraith.*

NOEHREN, T. H. **Malaria in Panama.** *U.S. Nav. Med. Bull.* 1946, June, v. 46, No. 6, 877–84, 1 chart. [10 refs.]

This paper recounts the experience of a Naval Medical Officer during 20 months in Panama, and is based on the study of 147 patients with malaria treated at a Naval Hospital. Only 42 of these patients were admitted to hospital with a diagnosis of malaria; 64 were sent with "diagnosis undetermined, possibly malaria"; the remainder were sent to hospital with diagnoses not suggesting malaria. During the same period 49 other patients were admitted to hospital with diagnoses suggesting malaria, but they were found to be free from malaria infection.

The most prominent and characteristic symptoms of the malaria patients were fever, retrobulbar headache, low back pain, perspiration of unusual odour, sudden malaise and anorexia. A combination of any four of these symptoms is highly indicative of malaria.

Cases of malaria were most frequent at the beginning and at the end of the wet season, though infection may be acquired in any month. The rainy season in Panama begins early in May and continues to December. Many patients gave a history of exposure to infection at known endemic places.

Tropical fevers of uncertain origin may simulate malaria. The classical symptoms of malaria are not infrequently absent in proved malaria cases in Panama. *Norman White.*

KITCHEN, S. F. & PUTNAM, P. **Observations on the Character of the Paroxysm in Vivax Malaria.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, Mar., v. 5, No. 1, 57–78, 5 figs.

This is an analysis of the febrile reactions of 70 white patients with neurosyphilis who were infected by mosquito bite with the McCoy strain of *P. vivax*.

The onset of *P. vivax* attacks may be marked by a few days of remittent fever, or of quotidian or tertian fever, or by a combination of both. Most attacks continue with quotidian periodicity. Intermittent fever from the beginning is apt to herald shorter attacks than initial remittent fever.

A rigor indicates a severe paroxysm and a greater susceptibility of the patient. Only 51 per cent. of the paroxysms in attacks of less than 3 weeks' duration were ushered in by rigors, as compared with 71 per cent. in longer attacks. The mean maximum temperature of 654 paroxysms with rigors was 1·7°F. higher than that of 346 rigorless paroxysms. An average of 5 days' clinical activity preceded the first rigor. The mean parasite density at the time of the first rigor was 4,012 per cmm. as compared with 274 on the day of first paroxysm. The mean duration of 654 rigors was 52 minutes. The patient's temperature was below 100°F. at the onset of 71·6 per cent. of the rigors. A mean increase in temperature of 4·2°F. was observed during the rigor. The highest mean maximum temperature in the course of 51 attacks was reached on the 7th day following onset; the mean maximum parasite density on the 9th day. Eighty-one per cent. of the 654 rigors occurred during the afternoon hours.

Norman White.

CHRISTIANSON, H. B., GORDON, H. H., DANIELS, W. B. & LIPPINCOTT, S. W. **Afebrile Parasitemia in Imported Vivax Malaria.** *Amer. J. Pub. Health.* 1946, July, v. 36, No. 7, 759–61.

Because of the proved transmissibility of some imported strains of *P. vivax* malaria to American mosquitoes, the question arises as to the frequency of patients who, without symptoms, may harbour gametocytes and be infective to mosquitoes.

The authors studied 200 patients at Harmon General Hospital, Longview, Tex., who were under observation for relapse, following proven previous relapses of *vivax* malaria of Pacific or Mediterranean origin.

Their blood was examined for malaria parasites twice weekly. If thick films were positive the patient was admitted to a ward, and thick and thin blood films taken at 12- or 24-hour intervals.

Oral temperatures were taken 4 times daily and daily records of symptoms were kept. No patient was treated unless his temperature exceeded 100°F. or until he had afebrile parasitaemia for 7 days.

Positive smears were found in 81 patients who were afebrile. Of these, 68 developed fever over 100°F. within 1 to 7 days after admission: they were treated for malaria. Only 13 of the 81 patients had parasitaemia without fever for 7 days.

The occurrence of gametocytes is shown in the following table :—

The Occurrence of Gametocytes in Routine Blood Smears of 81 Patients with Afebrile Relapses of Vivax Malaria.

	Patients who developed Fever			Patients without Fever for 7 days		
	Pacific	Mediter-ranean	Total	Pacific	Mediter-ranean	Total
Source of Malaria ...	53	15	68	8	5	13
No. of patients with gametocytes ...	3	4	7	1	3	4
Percentage of 81 patients with gametocytes ...	—	—	9	—	—	5
Total smears examined	—	—	203	—	—	87
Percentage of smears with gametocytes ...	—	—	3	—	—	7
Average days without fever	—	—	2	—	—	7

It will be noted that 8 (13 per cent.) of the relapses of Pacific malaria went 7 days without fever, as compared with 5 (25 per cent.) of the Mediterranean relapses.

Gametocytes developed in 11 (14 per cent.) of patients, and these occurred in 3 of the 5 afebrile Mediterranean relapses and in only 1 of the 8 afebrile Pacific relapses.

The authors consider that it is fair to conclude that most of the patients (85 to 95 per cent.) whose relapse was first recognized by blood examination probably constituted little menace so far as natural spread of the disease is concerned, since—unlike indigenous tropical peoples who often have parasitaemia without symptoms—they would be promptly treated, as controlled troops. Nevertheless, as the authors point out, this optimism does not dispense with the need for vigilant standards of mosquito control in peacetime.

H. J. O'D. Burke-Gaffney.

FISCHER, W. J. H., Jr. & YORK, C. L. **Quartan Malaria occurring subsequent to a Blood Transfusion. Report of a Case.** *New England J. of Med.* 1946, Sept. 19, v. 235, No. 12, 411–13, 1 fig.

"A case of quartan malaria, caused by *Plasmodium malariae*, in a native of New England subsequent to the transfusion of stored blood is reported. The three donors involved gave past histories of malaria forty, thirty-six and forty-two years previously, but blood films failed to reveal malarial parasites.

"The course of the illness, the parasite densities attained, the white-cell counts and the response to quinacrine therapy are discussed.

"Plasma, total blood and erythrocyte volumes, determined with the dye T-1824, were essentially the same during a paroxysm as during convalescence."

SPRAGUE, H. B. **The Effects of Malaria on the Heart.** *Amer. Heart J.* 1946, Apr., v. 31, No. 4, 426–30. [12 refs.]

The author reviews the literature concerning the effects of malaria on the heart. His own experience with several thousand cases of malaria occurring in the armed forces of the United States, and contracted in the Pacific area, leads to the conclusion that the possibility of cardiac damage being caused by recurrent malaria is extremely remote. He has observed neither death due to acute cardiac lesions, nor any proved cardiac disease, among such patients. A series of 50 cases of recurrent malaria, all but one *P. vivax* infections, were studied electrocardiographically. *Norman White.*

KAPLAN, L. I., READ, H. S. & BECKER, F. T., with the collaboration of M. F. BOYD. **Homologous and Heterologous Strains of *Plasmodium vivax*: a Cross-Inoculation Study of Malaria Strain Immunity.** *J. Lab. & Clin. Med.* 1946, Apr., v. 31, No. 4, 400–408.

The return to the U.S.A., in increasing numbers, of white troops from the Pacific area, where they have been exposed to *vivax* malaria raises the question of immunity to malarial infection if malaria therapy for the treatment of neurosyphilis becomes necessary. It might be suggested that in these cases quartan malarial infection should be employed, but the longer incubation period and duration of the cycle and paroxysms associated with this parasite entails longer hospitalization, while there may be produced years of latency which may prove dangerous from the point of view of accidental transfusion malaria. On this account the investigation on immunity to strains of *vivax* malaria described in this paper was undertaken. It is shown that parasites which were similar to those producing an original infection gave rise to infections whose duration averaged only 10·5 per cent. of the duration of the original infection. Re-infected patients thus showed a homologous immunity. When such patients were re-inoculated with dissimilar strains the duration of infection averaged 74·3 per cent. of the duration of the original infection and revealed heterologous immunity. In seventy-eight patients who had had no previous malaria, the prepatent periods and the incubation period after intravenous inoculation varied inversely with the dosage of parasites employed. From the results of the investigation it seems desirable to re-inoculate with heterologous strains of *P. vivax* patients who experience only modified types of the original infection (five to eight paroxysms). In this manner it will be possible to carry out adequate therapeutic courses of infection and to avoid the disadvantages of quartan infections. *C. M. Wenyon.*

QUEVAUVILLER, A. L'élimination de la quinine injectée au lapin est ralentie par un "véhicule-retard", le subtosan. [**Diminished Quinine Elimination in Rabbits, produced by a "Retarding Substance", Subtosan.**] *Rev. Paludisme et Méd. Trop.* 1946, Oct. 15, v. 4, No. 29, 225–8, 1 fig.

HERTZBERG, R. **Quinine Amaurosis: a Report of a Case.** *Med. J. Australia.* 1946, July 20, v. 2, No. 3, 92–3.

The author believes this to be the first case of quinine amaurosis among Australian soldiers in the late war.

The patient's history, chronologically, was as follows:—

Jan. 28th, 1946	10 grains of quinine sulphate (one dose of *Mist. Quininae*) for benign tertian malaria.
,, 29th ,,	30 grains of quinine sulphate.
,, 29th ,, (evening)	Vision blurred.
,, 30th ,,	On waking, was blind. 10 grains of quinine sulphate before he was medically examined: then quinine stopped and "Atebrin" given.
,, 31st ,,	Vision commenced to return, after 24 hours' blindness.
Feb. 3rd ,,	Ophthalmological examination: visual acuity, 6/9 in both eyes; pupils dilated and immobile; oedema at both maculae, but no other changes in the fundi; the fields were full (10/330 white).
,, 5th ,,	Additional changes in both fundi; disks pale, especially the right; arteries attenuated, and tended to become buried; no changes seen in the fields (10/330 white, red, blue).
,, 14th ,,	Patient stated that up to two days earlier he had difficulty in finding his way in the dark. Examination showed no new changes.
,, 21st ,,	Pupils normal in size and reactions; visual acuity 6/9 in the right eye and 6/6 in the left; oedema at maculae disappeared; vessels still attenuated and right disk pale.
Mar. 4th ,,	(Five weeks after onset); visual acuity 6/6 in both eyes; no new changes in the fundi; the fields were full (2/1,000 white).

The author quotes cases in the literature showing that visual symptoms may occur not only after doses of quinine similar to those in this case, but also following small dosage, *e.g.* 1·0 and 1·25 grains. Blindness following massive doses has also been reported and the author quotes the typical results described by MCGREGOR and LOEWENSTEIN [this *Bulletin*, 1945, v. 42, 91].

The author agrees with the writers quoted that the primary cause of quinine amblyopia is probably due to the action of the drug on the retinal nerve elements and that the purely vascular theory should be abandoned. "The changes in the retina may be so profound as to resemble the picture produced by occlusion of the central artery of the retina". The element of vaso-constriction is probably secondary.

In treatment, the important measure is rapid elimination of the quinine: but in the present case, the author did not see the patient until more than three days after quinine had been stopped. Expectant treatment was therefore carried out, and vitamin B administered. Recovery, as indicated above, was complete. *H. J. O'D. Burke-Gaffney.*

ROTENBURG, S. S. [**Treatment of Malaria with Acriquine by Administration of a Single Massive Dose on the First Day (0·3 gm. per os and 0·3 gm. intramuscularly).**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 4, 62–70, 1 fig. [In Russian.]

The author had previously made observations on the excretion of acriquine [=mepacrine] in urine after administration by mouth and by intramuscular injection, and has demonstrated that the therapeutic effect is higher when acriquine is introduced in a single massive dose of 0·6 gm. (0·3 gm. by mouth and 0·3 gm. intramuscularly, administered simultaneously). Under these conditions the concentration of acriquine reaches a sufficiently high level in urine during the first hours and is maintained in the course of the first day of treatment, whereas after oral administration (even in a dose of 0·6 gm.) a sufficient concentration is attained only during the second half of the first day of treatment. On the other hand, if acriquine is introduced only intramuscularly, an adequate concentration is reached rapidly but is retained only for 8–12 hours after the injection.

In the present paper, the author records the results of experimental treatment of 398 patients suffering from malignant and benign tertian malaria. Of these, 269 were given a single massive dose of 0·6 gm. on the first day, as described above, followed by doses of 0·3 gm. on the second and third days. The remaining 129, who served as controls, were treated by one of the following methods:—(*a*) 0·6 gm. acriquine given by mouth, in two doses, on the first day, and 0·3 gm. daily on the second, third and fourth days; (*b*) daily dose of 0·3 gm. by mouth during 5 days, and (*c*) daily dose of 0·3 gm. intramuscularly during 5 days. The subsequent cycles of treatment were the same in all cases, *viz.* 0·3 gm. daily for three days with intervals of ten days between the cycles.

The results have shown that the method of massive administration of acriquine on the first day (simultaneously by mouth and intramuscularly) was superior to all the others, as regards the time required to suppress the symptoms and to clear the peripheral blood of the parasites. The second place, from the point of view of therapeutic effect, was occupied by the method in which the massive treatment was carried out in two doses, given during the first day. In all these courses of treatment, no relapses occurred, provided the intervals between the cycles did not exceed 10–12 days.

The massive method of treatment has the advantage over the others in that the number of days (3) and the amount of drug used (1·2 gm.) in the course of the first cycle are reduced without affecting the frequency of relapses in those cases, in which the intervals between the cycles were unduly prolonged. Moreover, this treatment was not accompanied by any side-effects.

C. A. Hoare.

ANN. TROP. MED. & PARASIT. 1946, July, v. 40, No. 2, 215–18. **Prolonged Oral Administration of Mepacrine. III. The Clinical Effects in Women.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

This paper is a continuation of the reports on work carried out during the war to study the effect of prolonged administration of mepacrine to volunteers. One hundred and nine women students were divided into five groups, those who received 0·6 gm. mepacrine weekly, or 0·4 gm. weekly (3 groups on different régimes), and a control group who were given a placebo. After three months, all the volunteers were given 0·1 gm. mepacrine daily (0·7 gm. weekly). When equilibrium had been reached the mean plasma concentrations in these volunteers 24 hours after taking mepacrine [*i.e.* presumably just before the next dose] were 25 to 35 μgm. per litre. Twelve volunteers had mild gastro-intestinal symptoms which disappeared spontaneously, although the mepacrine

was continued. Three of the volunteers developed psychotic disturbances, but two of these were almost certainly not due to mepacrine, and the other one may or may not have been due to it. No other symptoms of consequence occurred; the weight and the blood picture were unchanged. Menstruation was not disturbed. Yellow staining of the skin occurred, especially on the parts exposed to sunlight, but this became masked by sunburn in half the cases.

F. Hawking.

Ann. Trop. Med. & Parasit. 1946, July, v. 40, No. 2, 181–9, 4 figs. **Distribution of Mepacrine in Blood.** [Army Malaria Research Unit, Oxford (Maegraith, B. G., *et al.*).]

This is a confirmation of the work of Shannon *et al.* [this *Bulletin*, 1945, v. 42, 343]. The mepacrine concentration in the various constituents of the blood was measured by Masen's method [this *Bulletin*, 1945, v. 42, 8].

Examinations were made on 8 subjects who had received mepacrine by various régimes and who had different white cell counts. The plasma contained 3–16 per cent. (usually 8–14 per cent.) of the total amount of mepacrine present, the red cell layer contained 8–35 per cent. (usually 11–13 per cent.) and the white cell layer contained 49–89 per cent. (usually 72–82 per cent.). Typical concentrations of mepacrine in μgm. per litre were :—

whole blood	208
plasma	60
red cell layer	40
white cell layer	9,600

It is not known whether the mepacrine in the white cell layer is in the white cells themselves or in the platelets. The concentration in the plasma is a better indication of the concentration in the red cells than is the concentration in whole blood. A patient with leukaemia (white cell count 200,000 per cmm.) was given 0·1 gm. mepacrine daily for 14 days. The mepacrine concentration in the plasma was only 60 μgm. per litre, but the concentration in the whole blood rose to 5,000 μgm. per litre; this abnormally high concentration was due to the increased white cell count. A second leukaemic patient gave evidence of the same phenomenon.

F. Hawking.

Arch. Intern. Med. 1946, July, v. 78, No. 1, 64–107, 24 charts. [Refs. in footnotes.] **Plasma Quinacrine Concentration as a Function of Dosage and Environment.** A Joint Report of the Armored Medical Research Laboratory, Fort Knox, Ky., and the Commission on Tropical Diseases, Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, United States Army.

This is the record of a very thorough and important investigation carried out in America during the war, in order to determine the plasma mepacrine levels in large groups of young men on various prophylactic or therapeutic régimes. It is difficult adequately to reproduce in an abstract, and the original should be consulted by those interested in the subject. Altogether, 250 subjects were used in this work. The plasma mepacrine concentrations following the administration of a single oral dose of 0·2 gm. to men who had already received varying amounts of mepacrine are shown in Fig. 1.

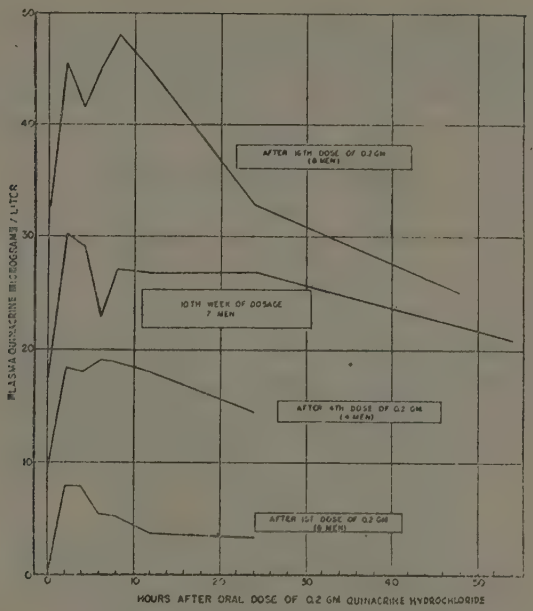

PLASMA QUINACRINE MICROGRAMS / LITER
AFTER 16TH DOSE OF 0.2 GM (8 MEN)
10TH WEEK OF DOSAGE 7 MEN
AFTER 4TH DOSE OF 0.2 GM (4 MEN)
AFTER 1ST DOSE OF 0.2 GM (8 MEN)
HOURS AFTER ORAL DOSE OF 0.2 GM QUINACRINE HYDROCHLORIDE

Fig. 1.—Postabsorption curves of plasma quinacrine concentration following 0·2 gm. dose.

Most of the rise occurs in the first two hours, the peak is reached in 2 to 8 hours, and then there is a gradual decline in the concentration. (All plasma concentrations are expressed as mepacrine base, and all oral doses as mepacrine hydrochloride.)

The (geometric) mean plasma level of a group of men taking 0·6 gm. mepacrine weekly is shown in Fig. 2.

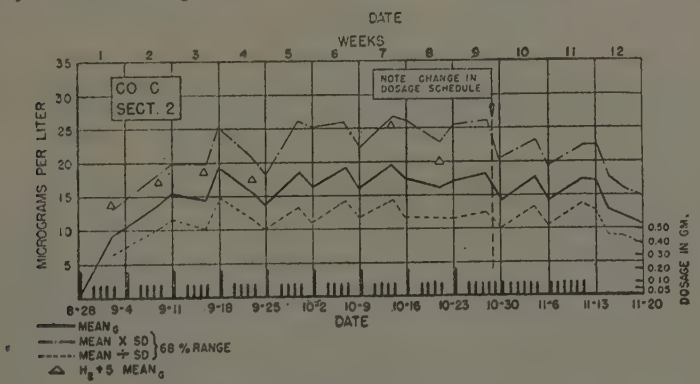


Fig. 2.—Mean$_G$ plasma quinacrine levels of a group of men receiving 0·6 gm. per week.

The plasma level rises gradually during the first 3–6 weeks, after which it reaches a steady level or " plateau " which continues until the dosage is altered

or discontinued. When equilibrium is reached, the mean plasma level is 30 microgm. per litre for each 1 gm. taken during one week.

If priming doses of mepacrine are given, *e.g.* 0·3 gm. daily for the first 6 days, the plasma concentration rises much more quickly and then subsides to the usual level, Fig. 3.

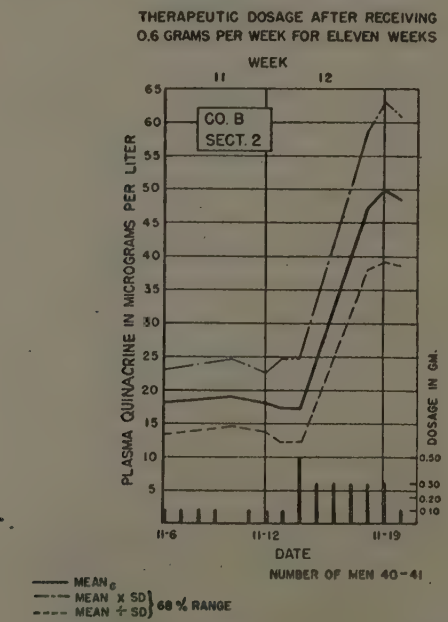


Fig. 3.—Plasma quinacrine levels obtained with different priming doses (maintenance dosage, 0·6 gm. per week).

Men who had received 0·4 or 0·6 gm. weekly for eleven weeks were then given a therapeutic course consisting of 0·5 gm. on the first day followed by 0·3 gm. on each of the next five days. The resultant mean plasma concentration is shown in Fig. 4.

When the administration of mepacrine was discontinued, the plasma level fell gradually by the usual type of " die-away curve ".

There is considerable individual variation of plasma level among the men of a group subjected to the same dose-régime ; this variation is distributed logarithmically. Also there was a small group of men who showed abnormally high plasma levels and another group (comprising about 7 per cent. of the total) who showed abnormally low plasma levels. This group with low plasma levels is of great practical importance ; for military purposes it was necessary to set the dose-régime of mepacrine at a level which would be high enough to raise the plasma level even of this group to a height which would be high enough to prevent malaria.

The mean plasma mepacrine in a group of subjects can be calculated from two principles, *viz.* (1) each gramme of mepacrine hydrochloride ingested raises the plasma level by 23·2 microgm. per litre ; and (2) there is a loss of 10 per

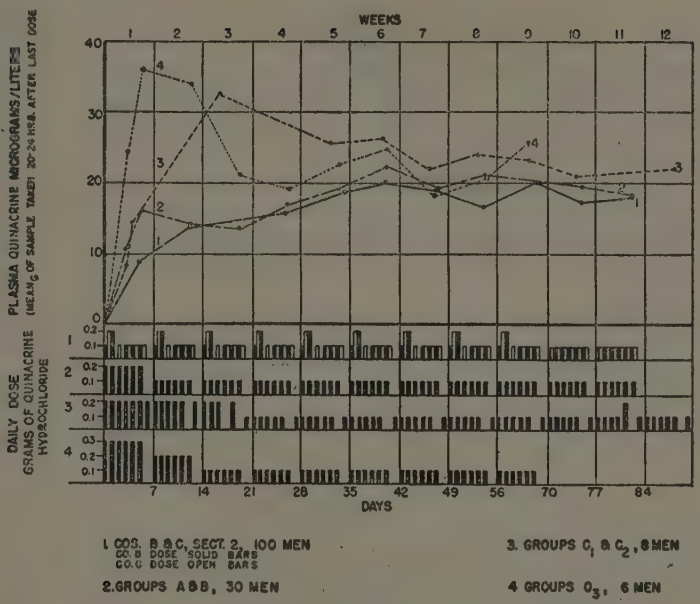

WEEKS
1 2 3 4 5 6 7 8 9 10 11 12
PLASMA QUINACRINE MICROGRAMS/LITRE (MEAN$_G$ OF SAMPLE TAKEN 20-24 HRS. AFTER LAST DOSE
40
30
20
10
0
DAILY DOSE GRAMS OF QUINACRINE HYDROCHLORIDE
0.2
0.1
0.3
7 14 21 28 35 42 49 56 70 77 84
DAYS
1. COS. B & C, SECT. 2, 100 MEN
CO. B DOSE SOLID BARS
CO. C DOSE OPEN BARS
2. GROUPS A & B, 30 MEN
3. GROUPS C_1 & C_2, 8 MEN
4 GROUPS O_3, 6 MEN

Fig. 4.—Mean$_G$ plasma quinacrine levels of a group of men receiving therapeutic dosage for one week.
[Reproduced from *Archives of Internal Medicine*.]

cent. of the plasma concentration each day. When administration is discontinued, the level drops by 10 per cent. each day.

A hot humid environment (artificial " jungle ") did not affect the absorption and storage of mepacrine as described above. No toxic effects were observed on any of the suppressive dose-régimes, but on the therapeutic doses one man had an epileptiform seizure at the fifth day ; on the 6th day his plasma mepacrine level was 108 microgm. per litre. Administration was continued throughout the seven-day regimen and no further incident occurred. The skin of these subjects was stained yellow, but the intensity of the colour, or the fluorescence of the skin and nails, could not be correlated with the plasma mepacrine levels.

F. Hawking.

Ann. Trop. Med. & Parasit. 1946, July, v. 40, No. 2, 173–80. **Mepacrine in Animal Tissues.** [Army Malaria Research Unit, Oxford (Maegraith, B. G., *et al.*).]

This paper describes further results obtained during wartime investigation on the pharmacology of mepacrine, other parts of which have already been abstracted in this *Bulletin*.

A dog weighing 7·7 kgm. was given 2·5 gm. mepacrine by mouth (apparently during several days) and was killed 5 days after the last dose ; the mepacrine content of the tissues (μgm. per gm.) was :—liver 52, spleen 54, lung 60, kidney 23, heart 16, brain 4, muscle 11, pancreas 79, and suprarenal 29. Two other dogs showed a similar distribution. In three rats the concentration in the liver was relatively greater than this in comparison with the concentration in the other organs. When dogs which had received mepacrine by mouth were given

an intravenous injection of the compound, the concentrations in the lung and kidney were greatly increased 10 minutes later, the concentrations in heart and spleen were moderately increased, while that in the liver showed little change ; by 24 hours the concentrations in all these tissues had returned to their previous levels. In a pregnant dog, mepacrine passed through the placenta and the concentrations in the foetal organs were about ⅓ to ½ of those in the maternal organs. The bile in the gall bladder of these dogs contained considerable amounts of mepacrine (4 to 43 mgm. per litre) ; but much of this mepacrine might have been re-absorbed as it passed down the intestine rather than have been excreted. When rats were given oral doses of mepacrine, the concentrations in the different organs increased steadily during the first 6 hours, but the relative distribution between the different organs remained unchanged.

Various studies were also made on volunteers. The concentration of mepacrine in the sweat was about the same as that in whole blood, but the amount excreted by this route is negligible. The saliva contained concentrations approximately the same as in whole blood. The concentration in the semen (400–1,100 μgm. per litre) was 2–4 times as high as that of the blood. The concentration in the bile (measured in two patients with biliary fistulae) was 2–3 times as high as in the whole blood, but it was much less than that in the urine ; the total amount excreted in the bile (much of this may have been re-absorbed in the intestine) was about one-fifth of that in the urine. Human hair contained up to 85 μgm. mepacrine per gm. ; dark hair contained more than light hair. A patient suffering from thrombocytopenic purpura was given 0·1 gm. mepacrine for 14 days, and the spleen was removed on the 15th day ; it contained 47 μgm. mepacrine per gm. . . . . *F. Hawking.*

Dimson, S. B. & McMartin, R. B. **Pamaquin Haemoglobinuria.** *Quart. J. Med.* 1946, Jan., v. 15, No. 57, 25–46. [30 refs.]

The observations recorded are based on 13 cases of haemoglobinuria that occurred among 10,000 Indian troops who had been given pamaquin during "blanket treatment", and 5 cases of haemoglobinuria that developed while 8,000 other Indian troops were undergoing the routine army treatment for malaria—quinine, mepacrine and pamaquin successively. "Blanket treatment" was the course of treatment given to men withdrawn from a malarious area to one that is non-malarious, and consisted of mepacrine 0·1 gm. thrice daily for 5 days, rest for 2 days, then pamaquin 0·01 gm. thrice daily for 3 or 5 days. Three of the patients who had received blanket treatment died. Detailed information concerning possible aetiological factors and the results of blood examinations in the 18 cases of haemoglobinuria are given in tabular form. Clinical and post-mortem findings were identical with those described in classical blackwater fever.

With respect to reaction to pamaquin, patients may be divided into four groups : (*a*) those in whom there is no evidence of intravascular haemolysis ; (*b*) those who show only a positive Schumm's test and in whom symptoms are vague or absent. (Schumm's test consists of the spectroscopic examination of plasma to which fresh concentrated ammonium sulphide has been added. In positive cases the α band of ammonium haemochromogen can be seen sharply defined at 558μμ. The test is specific for methaemalbumin.) ; (*c*) those who have haemolysis as shown by a positive Schumm's test, hyperbilirubinaemia, increase in urobilinogen, but no frank haemoglobinuria. These are *formes frustes* of haemoglobinuria and the signs and symptoms are jaundice, dark urine, anorexia, epigastric pain, vomiting, slight fever, weakness, giddiness,

dyspnoea, palpitations and thirst ; (*d*) those in whom frank haemoglobinuria occurs, with signs and symptoms identical with those of classical blackwater fever.

Over-susceptibility to pamaquin is believed to be the determining factor in producing the haemoglobinuria, and the previous administration of mepacrine an important contributory cause. *Norman White.*

AGRESS, C. M. **Atabrine as a Cause of Fatal Exfoliative Dermatitis and Hepatitis.** *J. Amer. Med. Ass.* 1946, May 4, v. 131, No. 1, 14–21, 6 figs.

The author points out that almost no serious reactions are caused by atebrin (mepacrine), other than psychosis. He quotes 5 cases of severe hepatitis and exfoliative dermatitis, following the use of atebrin for malaria, in Chinese patients in the India-Burma theatre, but emphasizes that these represent a very small incidence, less than 1 in 3,000. He has only found one case in the literature of exfoliative dermatitis following atebrin, and no case of hepatitis.

In the present series, 3 of the 5 patients died. None of these cases occurred during a period when infectious hepatitis was present in other patients.

Detailed clinical descriptions of the 5 cases are given and it is pointed out that the specificity of the condition was not fully realized until the fifth case was encountered.

Clinically and *post-mortem* the cases were remarkably similar. Prominent features were the following :—

1. A rash appearing from the 2nd to the 10th day on as little as 0·1 gm. of atebrin in a sensitized patient, though larger doses were usually necessary. The rash was scarlatiniform, maculo-papular or a dry scaling, beginning on the face and involving the whole body, and being followed by desquamation. Exfoliation of the tongue and conjunctivitis also occurred.

2. Jaundice resulting from hepatitis sometimes appeared several days after the eruption. This was accompanied by high septic fever, leucocytosis as high as 40,000 per cmm. and eosinophilia up to 45 per cent.

3. Albuminuria, and bile, but not urobilinogen, in urine. The liver enlarges at first, but rapidly shrinks.

4. Mental clouding, a constant feature.

5. Generalized discrete adenopathy as the desquamation progresses to a thick leathery skin.

6. Gradual deterioration, wasting, often eczematoid skin changes, progressive liver failure, and death in coma in the 3rd to the 5th week.

7. The following *post-mortem* changes were found : exfoliative dermatitis ; evidence of severe hepatitis, or necrosis producing a small wrinkled liver with mottled degenerative areas ; acute cloudy swelling of the kidneys with bile staining ; moderate adenopathy ; splenomegaly typical of malarial infection.

The author presents the following major points in favour of atebrin as the aetiological agent :—

1. It was the only drug common to all cases.

2. Positive patch tests to atebrin, with negative controls, were obtained in 4 of the 5 cases. Control patients with severe dermatitis produced only 8·3 per cent. positives.

3. Autopsy and laboratory studies revealed no other aetiological agent.

4. The patients were admitted for totally unrelated diseases, but their terminal manifestations were strikingly similar.

5. Exfoliation was produced accidentally in the first patient with only 0·1 gm. of the drug.

6. The fifth patient was well controlled and would seem to leave no doubt that atebrin was the aetiological agent.

In view of the wide clinical use of atebrin, investigations were made to devise a sensitivity test, which would be useful in predicting and preventing reactions and as a diagnostic procedure. A number of methods were tried, and it was found that a patch test prepared from 0·1 gm. of atebrin [tablets, " atabrine dihydrochloride "] to 10 cc. of tap water gave the best results when read in 24 hours. Control tests were carried out on the opposite arm, with preparations of other drugs.

This procedure only gave 3 per cent. false positive reactions with normal skins, and 8·3 per cent. false positive reactions in patients with existing dermatitis.

The author states that the toxic reaction following atebrin which he has described may occur from extreme sensitivity on as little as 0·1 gm. of the drug, or may be the result of prolonged and repeated administration.

He considers that prompt recognition and treatment of these complications with such detoxifying agents as vitamin C and liver extract, intravenous glucose and plasma, together with withdrawal of the drug, may prove to be life-saving, although the mortality in his 5 cases amounted to 3 out of 5 patients.

[The extremely detailed clinical notes of the cases are not only fully informative in themselves, but demonstrate strikingly the patient and careful investigations which led to the recognition of the common aetiological cause.]

H. J. O'D. Burke-Gaffney.

Campbell, K. N. & Kerwin, J. F. **Studies in the Quinoline Series. II. The Preparation of some Dialkylaminomethyl-4-Quinoline Methanols.** *J. Amer. Chem. Soc.* 1946, Sept., v. 68, No. 9, 1837–40. [Refs. in footnotes.]

Campbell, K. N., Helbing, C. H. & Kerwin, J. F. **Studies in the Quinoline Series. V. The Preparation of some α-Dialkylaminomethyl-2-Quinoline-methanols.** *J. Amer. Chem. Soc.* 1946, Sept., v. 68, No. 9, 1840–43. [Refs. in footnotes.]

Campbell, K. N., Sommers, A. H., Kerwin, J. F. & Campbell, Barbara K. **Studies in the Quinoline Series. VI. The Preparation of some Substituted Lepidylamines.** *J. Amer. Chem. Soc.* 1946, Sept., v. 68, No. 9, 1851–2.

Campbell, K. N., Kerwin, J. F., LaForge, R. A. & Campbell, Barbara K. **Studies in the Quinoline Series. VII. The Preparation of some α-Dialkyl-aminomethyl-8-Quinoline Methanols.** *J. Amer. Chem. Soc.* 1946, Sept., v. 68, No. 9, 1844–6. [Refs. in footnotes.]

Spinks, A. & Tottey, Mary M. **Studies on Synthetic Antimalarial Drugs. XVI. The Absorption, Distribution and Excretion of 2-*p*-Chlorophenyl-guanidino-4-β-Diethylaminoethylamino-6-Methylpyrimidine (3349) in Experimental Animals.** *Ann. Trop. Med. & Parasit.* 1946, July, v. 40, No. 2, 145-52, 6 diagrams. [13 refs.]

The authors, using a turbidimetric or colorimetric method for the estimation of the compound 3349 [this *Bulletin*, 1946, v. 43, 398], have already shown that the behaviour of this drug in the body resembles that of mepacrine. The present experiments, based on such behaviour and on that of quinine, were carried out in seeking a guide to the mechanism of antimalarial action of the drug. Rats and mice were used as experimental animals. After oral administration to rats of 100 mgm. base per kilo (or 25 mgm. per kilo. by the intravenous route) the amounts of drug present in the blood, plasma and cellular elements, as well as in various tissues, were determined. It was found that the drug is slowly absorbed and that the blood or plasma concentration remains low,

being considerably higher in the cellular elements ; while in tissues it is several hundred times as high. The highest concentrations were found in liver or lung, depending on the route of administration. The drug was still detectable in tissues six days after a small intravenous dose. It was excreted to a small extent in the urine but mainly in the faeces. Even when the drug was given intravenously, excretion into the small bowel was rapid, about half of it reaching this site in the bile. From recovery data it appeared that only negligible amounts of the drug were metabolized ; its behaviour in the two species of animal was similar, and, in general, resembled that of mepacrine. During comparative experiments with quinine, a sensitive method for the estimation of that drug in plasma was developed ; this consisted in extraction of the alkaloid from basified plasma, with a benzene-ethanol mixture. These solvents were in turn extracted with dilute sulphuric acid, and comparisons made with standards in a fluorimeter using a blue filter. *J. D. Fulton.*

SPINKS, A. **Studies on Synthetic Antimalarial Drugs. XVII. The Absorption, Distribution and Excretion of N_1-*p*-Chlorophenyl-N_5-Methyl-N_5-Isopropyl-biguanide (4430) in Experimental Animals and Man.** *Ann. Trop. Med. & Parasit.* 1946, July, v. 40, No. 2, 153–62, 6 diagrams.

Similar methods to those described in the preceding abstract have been used to determine the fate of the antimalarial compound 4430 in rats and mice. Doses of 80 and 20 mgm. per kilo. were given by the oral and intravenous routes respectively. The drug was estimated by the methods previously described by the author [this *Bulletin*, 1946, v. 43, 398, 400]. It was found to be rapidly absorbed from the alimentary tract, maximum concentrations of 1·5 and 0·45 mgm. per litre being reached in blood and plasma respectively, while the concentrations in tissue were much higher, but soon fell. Five days after administration, 4430 was still detectable in urine, in which it is excreted to a greater extent than quinine or mepacrine ; but only a small percentage of the administered dose was recovered from this source. Excretion into the small intestine from the blood occurs partly through bile. The amount recovered from faeces was less than in the case of 3349, described above, and this fact suggests that it had to some extent been metabolized. In rats, mice and rabbits the fate of the drug was approximately the same. In man the drug was rapidly absorbed after oral administration, and higher blood levels were reached than with similar doses of mepacrine. Maximal blood levels of 0·6 to 1·0 mgm. per litre were reached after the second or third oral dose of 200 and 400 mgm. respectively. Over a period of 5 days after administration to the human subject, approximately 25 per cent. of administered drug was recovered in urine. Regarding distribution and excretion, the properties of the drugs mentioned are roughly alike, but 4430 appears to have less affinity for cellular elements. These properties are believed to depend in part on variations in basic dissociation constants, and on the characters of the side chains. *J. D. Fulton.*

BARBER, H. J. & WRAGG, W. R. **Composition of the Antimalarial Drug R.63 and the Ing and Manske Hydrazine Hydrolysis of N-Substituted Phthalimides.** [Correspondence.] *Nature.* 1946, Oct. 12, 514.

WATSON, R. B. & RICE, Margaret E. **Notes on the Morbidity of naturally occurring Malaria.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, Mar., v. 5, No. 1, 7–12, 1 fig.

In 1941 the authors reported the results of mosquito-proofing of houses in three areas of the Tennessee Valley for malaria control [this *Bulletin*, 1942, v. 39,

436]. Morbidity data were collected by public health nurses who made weekly visits to all homes. The data then collected are now analysed in terms of duration of illness. The population concerned consisted of 2,159 persons, half of them whites, half negroes. Under similar or worse environmental conditions negroes suffered less illness from malaria than white persons, with regard both to total number of cases and to duration of illness. A blood survey, however, showed that negroes had a greater relative number of infections. *Norman White.*

Sergent, Ed. & Sergent, Et. Une simple et radicale " grande mesure anti-larvaire " contre les anophèles : le colmatage. [**Colmatage, a Simple and Radical Antilarval Measure.**] *Arch. Inst. Pasteur d'Algérie.* 1946, Mar., v. 24, No. 1, 24–8, 1 map.

This paper describes the successful use of *colmatage* in obliterating a large marsh which had been a prolific source of *Anopheles* and in reclaiming the land for agriculture. *Colmatage* consists in causing silt-laden waters to deposit their silt on lowlands.

The vast marsh of Ouled Mendil, near Birtouta in the Mitidja plain, which malaria had made uninhabitable for man and piroplasmosis for cattle, was handed over to the Pasteur Institute in 1929, for experiment in modern methods of reclamation. The marsh contained a pond 475 metres long, 100 metres wide, which offered facilities for mosquito breeding during the greater part of the year. The marsh itself was flooded for several months each year until midsummer. The marsh lies at the foot of the Sahel Hills, from which the heavy winter rains flow down ravines to a canal, to be discharged into the sea. The average rainfall is 760 mm. a year. This water is heavily laden with silt. A secondary canal was cut, which carried the water to a series of rectangular basins surrounded by banks 40 to 50 cm. high. In these, the silt was deposited and the clear water was drained from the last basin downstream. Each year the position of these basins was changed. In 5 years 245,000 cubic metres of silt were deposited on 35 hectares of land. The pond and marsh had disappeared. The reclaimed land is under profitable cultivation. *Norman White.*

Eads, R. B. **Vertical Drainage for Mosquito Control on a Solomon Island Base.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, Mar., v. 5, No. 1, 39–41, 1 fig.

In the level areas of the Solomon Islands there are numerous depressions, usually less than 100 yards square and from 4 to 10 feet deep. They are apparently of recent formation and may have been the result of earthquakes. The water they contain requires attention, though it is not very productive of anophelines.

A simple form of drainage gave good results. A hole six feet square was dug down to coral, some ten to twelve feet from the sink hole to be drained. The hole was deepened two or three feet more. A ditch one foot wide was then dug to connect the two. A screen was placed at each end of the ditch, which was filled with coral. By this means ponds 100 feet square and eight feet deep have been drained in a day. The depressions have remained dry for ten months. *Norman White.*

Wilson, D. Bagster. **Notes of some Investigations on Mosquito Larvicides.** *East African Med. J.* 1946, Aug., v. 23, No. 8, 239–45.

In an endeavour to improve larvicidal control of *Anopheles* in East Africa for military purposes certain materials were tested in the field, with the following results :—

1. Di-nitro-ortho-cresol. An effective insecticide against locusts which proved of no value as a mosquito larvicide.
2. Malachite, a copper mineral. An effective agent for the control of fresh-water snails but of no practical value as a larvicide.
3. Derris. The powdered root of *Derris elliptica* (2 lb. per acre), diluted with wood-ash, was found very effective, and most useful in irrigated vegetable gardens.
4. Gammexane. A dosage of 0·02 gramme per square yard (4 oz. per acre) in diesolene or used engine-oil was effective against the larvae of *Anopheles gambiae*; 0·05 gramme was lethal to all fauna. A similar dosage (0·02 gramme) of the crude powder in dust was not so effective.

The effectiveness of the anti-malarial oil mixture in use in East Africa was in doubt. After investigations based on the laboratory methods of DAVID [this *Bulletin*, 1943, v. 40, 16], the following mixture was finally adopted to rectify the main defect of lack of spreading power :—

Inland diesel	...	...	...	42 per cent.
Diesolene	...	...	...	31 ,,
Furnace oil	...	...	...	18 ,,
Power kerosene	...	...	...	9 ,,
Fatty acids	...	...	...	0·6 ,,

The spreading pressure is over 20 dynes per cm. and relative viscosity 1·00. Dosage of 5 gallons per acre kills 100 per cent. of larvae of *Anopheles gambiae*; the dosage usually quoted is 10 to 15 gallons per acre. [Similar difficulties were encountered in military malaria control work in West Africa. The use of DDT or gammexane in an oil of high spreading power will eventually replace the effective Malariol.] *R. Ford Tredre.*

WHITE, R. Senior, GHOSH, A. R. & RAO, V. V. **On the Adult Bionomics of some Indian Anophelines : with special reference to Malaria Control by Pyrethrum-Spraying.** *J. Malaria Inst. of India.* 1945, Dec., v. 6, No. 2, 129–215, 3 charts. [46 refs.]

This paper starts with a critical review of the published results achieved in India by the spray-killing of adult mosquitoes with pyrethrum insecticides. These results have been more successful against *A. culicifacies* than against *A. minimus*.

Over a period of eight months, July to February, a laboratory study in plugged tubes was made of the duration of the gonotrophic cycle in six species : *A. subpictus*, *A. vagus*, *A. culicifacies*, *A. fluviatilis*, *A. varuna*, and *A. minimus*. Only in July was digestion complete in 48 hours (average tube temperature 26°C.). In nearly every month *A. minimus* took from half to one day longer than did *A. fluviatilis* to complete digestion. A study was made of the relation of the digestive to the ovarian stages in *A. culicifacies* and in *Anopheles* of the *fluviatilis* group : very high correlations were found between abdomens in stages I–II, III–V and VI–VII, and ovaries in stages I, II–III and IV–V, respectively.

In 1937, Senior White showed that in the Chatikona area in the Jeypore Hills six species were concerned, in varying degree, in the transmission of malaria :— *A. culicifacies*, *A. fluviatilis*, *A. varuna*, *A. minimus*, *A. aconitus* and *A. jeyporiensis* [this *Bulletin*, 1937, v. 34, 627–8]. In the investigation now reported these six species were tested for the origin of their blood meals in each month of the year. The anthropophilic indices of 1,832 specimens, as found in houses, stables and empty shelters, of the six species were determined. The average anthropophilic index of *A. culicifacies* was 27·2, much higher than is

usual in India, but the species is negligible as a vector of malaria in the Jeypore Hills. Oöcysts have been found, but no sporozoites. Probably few if any of this species survive ten days. The three chief vectors, *A. fluviatilis*, *A. varuna* and *A. minimus*, had average anthropophilic indices of 84·2, 79·0 and 92·4, and sporozoite rates (in 1937) of 4·3, 6·1 and 4·4 respectively. *A. aconitus* is a comparatively rare species; it has been found once with oöcysts but never with sporozoites. Its average anthropophilic index was 15·5 (28·6 in houses). *A. jeyporiensis*, which had a much higher oöcyst rate than other non-vector species (sporozoites never found) had an anthropophilic index in houses of 27·8. It would seem that adult expectation of life is of importance in determining the vectorial potentialities of a species.

To study movement and longevity, experiments were made with stained mosquitoes. Mosquitoes were dusted with printers' coloured powders. A fallacy vitiated this work. Some of the dusted mosquitoes deposit some of the dust on cobwebs in the release hut; some of the unstained mosquitoes entering the hut come in contact with these webs, and thus the stained population is continuously augmented. Watery stains were subsequently employed and showed that a very high percentage of *A. fluviatilis*, *A. minimus* and *A. jeyporiensis* survived for over twelve days in the cold weather.

A. culicifacies remains in human dwellings after feeding until digestion is nearly complete. Vectors of the *fluviatilis* group leave the house when the cycle is only half complete, and are thus vulnerable for spray-killing for only one daylight period in each cycle.

Data on night catches in sprayed and unsprayed rooms are given. The entrance of *fluviatilis* is highest after midnight. Pyrethrum acts as a repellent to mosquitoes entering rooms.

Against the *fluviatilis* group spraying for six days each week is the most effective.

Further evidence is adduced that *A. varuna* covers more than one species or biological race. *Norman White.*

KARTMAN, L. & DA SILVEIRA, M. M. **Effect of Short Contact with DDT Residues on *Anopheles gambiae*.** *J. Econom. Entom.* 1946, June, v. 39, No. 3, 356–9, 2 figs.

The experiments described were done at Dakar, French West Africa, during July–September 1944. Females of *A. gambiae* were given short periods of contact with DDT by sucking them individually into a glass aspirator tube 10 mm. in diameter, on which a film of DDT had been deposited at a rate equivalent to 125 mgm. per sq. ft. After a short exposure, during which contact by legs and wings with the walls of the tube was ensured by its small diameter, the mosquitoes were blown out into a recovery cage. It was found that after 60-, 30-, and 5-second periods of contact, most of them showed toxic symptoms ten to thirty minutes later. The 30- and 60-second contacts caused over 95 per cent. mortality within eight hours after contact.

[While these highly lethal effects of short exposures are interesting, it should be remembered that the glass surface of the aspirator does not constitute a representative test; all the DDT would be on the surface, since glass is not permeable. The method of applying the DDT is not stated.] *J. R. Busvine.*

VISWANATHAN, D. K., RAO, T. R. & RAO, T. S. R. **The Behaviour of *Anopheles fluviatilis*. Part IV. Experiments on the Behaviour of Gravid Females.** *J. Malaria Inst. of India.* 1945, Dec., v. 6, No. 2, 243–5.

Fully gravid specimens of *A. fluviatilis* were dusted with gold or silver dust and liberated in a hut or a tent. Four experiments were made, during which

285 mosquitoes were so treated. Of these, 15 were found to return for a blood meal after oviposition, within a few hours of the time of release. Two others returned the following night.

Spray-killing of this species should be designed to destroy broods of 48 hours' and 72 hours' feeding cycles, irrespective of the season of the year. Spraying for two consecutive days, separated by one and two free days, alternately, is recommended, if concurrent antilarval measures cannot be carried out.

Norman White.

CARLSON, H. J., BISSELL, H. D. & MUELLER, M. G. **Antimalarial and Antibacterial Substances separated from Higher Plants.** *J. Bacteriology.* 1946, Aug., v. 52, No. 2, 155–68, 1 graph.

Previous workers have obtained extracts from a variety of higher plants, which show activity against micro-organisms. The present workers have prepared extracts from more than 200 species of wild and domestic plants, and have tested their value *in vitro* and *in vivo* against pathogenic and non-pathogenic organisms. In the preparation of the extracts, fresh plants were ground with sand, saline was then added, followed by filtration through gauze. The *p*H level was then adjusted to approximately 7. Other preparations were also made by extraction with organic solvents or by means of steam distillation. By *in vitro* methods it was found that the extracts of five plants (buttercup, sagebrush, dwarf waterleaf, mountain pasque and juniper) showed activity. Tests against a number of organisms were made by the Oxford cup method as well as in the vapour phase. In the malaria tests, blood infected with *P. gallinaceum*, containing a definite number of parasites, was mixed with an equal volume of extract and incubated for six hours at room temperature. Chickens two weeks old were then inoculated intravenously with the mixture, and were observed over a period of four weeks. The extracts of the five plants named proved lethal to the parasites under these conditions. Sagebrush and dwarf waterleaf extracts had also some action against the blood phase in chickens and apparently influenced the exoerythrocytic stage of the disease. Some extracts also possessed activity against bacteria, fungi, soil organisms and non-pathogenic protozoa. Mice infected with pneumococci were protected by mountain pasque extract. The extracts of sagebrush and waterleaf possessed anaesthetic properties for chickens and mice. *J. D. Fulton.*

CANTRELL, W. & JORDAN, Helen B. **Changes in the Infectiousness of Gametocytes during the Course of *Plasmodium gallinaceum* Infections.** *J. Infect. Dis.* 1946, Mar.–Apr., v. 78, No. 2, 153–9, 1 fig.

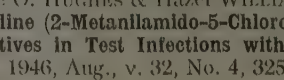
With a view to discovering the optimum moment for feeding *Aëdes aegypti* on chickens infected with *P. gallinaceum* in order to obtain the maximum oöcyst development, mosquitoes were fed at various stages of infection. It was found, as LUMSDEN and BERTRAM [this *Bulletin*, 1941, v. 38, 414] have previously noted, that the time of maximum infectivity did not always coincide with the peak of gametocyte number. In fact it was found that the maximum number of oöcysts occurred in mosquitoes fed on infected chickens the day before the peak of parasitaemia. On the day of the peak of parasitaemia, though gametocytes were considerably more numerous than on the previous day, they did not develop so readily in the mosquito. Thus, in mosquitoes fed on the day before the peak on two chickens, the ratio of gametocytes per 100 microscopic fields to oöcysts per mosquito was 37 and 77 respectively. At this time 10 per cent. of the red blood corpuscles were infected. On the following day, on which the peak of parasitaemia was reached, the ratio had fallen to 1·2 and 1. Certain changes in the appearance of many of the gametocytes were evident at the peak, and were increasingly evident after this. These changes

were vacuolation, raggedness of the edges, clumping of pigment and irregular staining. Several possible reasons for the declining infectivity are considered. The gametocytes may become senile and lose their ability to infect, they may fail to reach maturity on account of the blood being depleted of substance essential for their maturation in the chicken, or the blood taken up by the mosquito may lack the nutritive substances necessary for their development. In order to test the nutrient hypothesis, mosquitoes were fed on three chickens just before and just after transfusion with normal chicken blood. In the case of two of the chickens the oöcysts in the mosquito fed after transfusion were increased two or three times, but in the case of the remaining chicken there was no such increase. If the nutrient deficiency hypothesis would account for the reduction in the number of oöcysts it might be expected that there would be a simultaneous reduction in the average size of the oöcysts. This was found to be the case, for mosquitoes fed on the more heavily infected chickens had not only fewer, but also smaller, oöcysts. *C. M. Wenyon.*

Taliaferro, W. H. & Taliaferro, Lucy G. **Immunological Relationships of *Plasmodium gallinaceum* and *Plasmodium lophurae*.** *J. Infect. Dis.* 1945, Nov.–Dec., v. 77, No. 3, 224–48, 12 figs. [22 refs.]

Chickens were infected with *P. gallinaceum* or *P. lophurae*, and 3–5 or 7–8 weeks after the initial infection were tested for homologous or heterologous immunity to these two parasites. Similarly, chickens hyperimmunized by repeated superinfections were tested. The tests were carried out by injecting the immune or hyperimmune chickens intravenously with heavy doses of infected blood, and noting the time of disappearance of parasites from the blood. Chickens which had recovered from a *P. gallinaceum* infection or had been hyperimmunized against this species showed, when tested, a marked homologous immunity against *P. gallinaceum* and marked heterologous immunity against *P. lophurae*. On the other hand, chickens which had been treated with *P. lophurae* showed, when tested, marked homologous immunity against this species but only slight heterologous immunity against *P. gallinaceum*. The immunities were stronger after 8 weeks in chickens infected with *P. gallinaceum* and after 4 to 5 weeks in chickens infected with *P. lophurae*. In *P. gallinaceum* infections the immunity increases progressively over a long period, probably as a result of the persistence of a low-grade infection. It is not accelerated by superinfection with sporozoites, and is actually diminished by superinfection with blood stages of the parasite. On the other hand, with *P. lophurae* the immunity decreases as the infection progresses, and is increased by superinfection with blood stages. It is supposed that this difference is due to the constant absorption of antigen from the persisting low-grade infection in the case of *P. gallinaceum* and the rapid cessation of antigen absorption owing to the early development of latency in *P. lophurae* infections. In general, erythrocytic stages and sporozoites behaved similarly whether used for immunization or testing.
C. M. Wenyon.

Brackett, S. & Waletzky, E., with the technical assistance of Margaret Baker, Carrie O. Hughes & Hazel Williams. **The Antimalarial Activity of Metachloridine (2-Metanilamido-5-Chloropyrimidine) and other Metanilamide Derivatives in Test Infections with *Plasmodium gallinaceum*.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 325–39. [23 refs.]

Metachloridine,  , and some related compounds have been found effective in causal prophylaxis and in treatment of *P. gallinaceum* infections of chickens, provided they are given early enough.

In its rate of action, metachloridine appears to resemble sulphadiazine in this infection, as reported by the authors [this *Bulletin*, 1946, v. 43, 713]. Previously, COATNEY & COOPER [this *Bulletin*, 1945, v. 42, 353] had shown that certain sulphanilamides also acted as causal prophylactics. Maximum tolerated doses of metachloridine have, however, been found unable to effect a cure of established infections. In sporozoite-induced infections, drug treatment was started two days before inoculation and continued for 10 days. When sulphadiazine was used as the standard suppressive drug the estimation of activity was based on the length of prolongation of the incubation period. In blood-induced infections, quinine served as standard, and drug treatment was begun on the day previous to intravenous inoculation of infective material, and continued for 4 days thereafter. The number of parasites present in the blood of experimental animals was then expressed as a percentage of that in the controls. The drugs were given in diet to the birds, which were kept alternately in light and dark for three-hour periods. Splenectomy followed by examination of blood smears served as a guide to the presence of a latent infection. The details of drug estimation are described and were based on the methods of BRATTON & MARSHALL (*J. Biol. Chem.*, 1939, v. 128, 537). Metachloridine and its bromine and iodine isomers were the most active of 42 substances tested, and possessed much greater activity than the standard drugs. Only those with heterocyclic groups possessed antimalarial properties. The biological activity of sulphanilamides and metanilamides appears to be different as their activity against various organisms does not run parallel and the latter are not so readily antagonized by *p*-aminobenzoic, while *m*-aminobenzoic was able to antagonize only the less active members of the group and its activity was not specific. Metachloridine has a low toxicity for animals and has given encouraging results in human malaria, but was inactive against a number of other protozoan parasites. *J. D. Fulton.*

HUGHES, Carrie O. & BRACKETT, S. **The Prevention of Sporozoite-induced Infections of *Plasmodium cathemerium* in the Canary by Metachloridine.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 340–44.

Besides acting as a causal prophylactic against *P. gallinaceum* infections of chickens, metachloridine (see previous abstract) can prevent infection of canaries by sporozoites of *P. cathemerium* injected subcutaneously or intramuscularly. It is also effective against blood infections. The drugs here tested were given in drinking-water while the birds were maintained continuously in the light. Estimations of the blood-level of drugs and their activity were made as described above. The following is the author's summary :—

" 1. Metachloridine (2-metanilamido-5-chloropyrimidine) prevented sporozoite infections of *Plasmodium cathemerium* in four out of four canaries; 2-metanilamido-pyrimidine prevented infections in one out of three birds and greatly prolonged the incubation period in the other two ; while 2-sulfanilamido-5-bromopyrimidine has at best very slight activity.

" 2. All of these drugs suppressed blood-induced infections of *Plasmodium cathemerium* in the canary." *J. D. Fulton.*

SEELER, A. O. & OTT, W. H. **Studies on Nutrition and Avian Malaria. IV. Protein Deficiency.** *J. Infect. Dis.* 1945, Nov.–Dec., v. 77, No. 3, 181–4, 1 fig.

The authors have shown that a *P. lophurae* infection in chicks on a diet deficient in protein runs a more severe course than in chicks on a diet containing adequate protein. When chickens on a high protein diet are inoculated with

200 million parasitized cells per kgm. of body weight the resulting infection is mild, whereas in chickens on a protein-deficient diet the infections are severe, with a high mortality rate. Even when the protein deficiency did not bring about a decrease in the total serum protein, it nevertheless increased the severity of the infections. It was noted also that chickens on protein-deficient diets did not rid themselves of parasites as readily as did chickens on a high protein diet. It has recently been shown by CANNON and his collaborators that mammals suffering from hypoproteinaemia are unable to produce normal amounts of antibody in response to antigenic stimulus. It would seem probable that a failure to produce sufficient antibody may account, in part at least, for the effect of protein deficiency on avian malaria. *C. M. Wenyon.*

FALLIS, A. M. *Plasmodium circumflexum* **(Kikuth) in Ruffed Grouse in Ontario.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 345–53, 7 figs.

FLETCHER, D. E. & RIGDON, R. H. **Neurologic Manifestations associated with Malaria in Ducks.** *Arch. Neurology & Psychiatry.* 1946, Jan., v. 55, No. 1, 35–42, 4 figs. [14 refs.]

Ducks inoculated intravenously with heavy doses of blood infected with *P. lophurae* acquire heavy infections, in which as many as 450 of every 500 red blood corpuscles may harbour parasites. These ducks usually die before the tenth day. If smaller doses of infected blood are administered the infections produced are correspondingly milder, and recovery is more frequent. The infected ducks become pale and weak, the red cell count falling from two and a half millions to half a million. In the case of ducks which recovered after the crisis, malarial parasites disappeared completely from the circulating blood and the ducks recovered to such an extent that they were indistinguishable from ducks which had not been submitted to infection. However, a few weeks later the majority of these ducks showed signs of neurologic disturbances, such as ataxia, inco-ordination and disturbances of posture and equilibrium. It was found that severely infected ducks showed injury to the brain, spinal cord and peripheral ganglia and nerves. There was oedema of these tissues associated with focal areas of degeneration in the fibre tracts, extensive demyelination of the nerve fibres, pyknosis, oedema and fragmentation of the nerve cells. The nuclei and fibre tracts functionally associated with the cerebellum are the structures most extensively damaged. The suggestion is made that anoxia, which results from the anaemia and is later aggravated by vasomotor instability and circulatory failure, is the factor responsible for these pathological changes. *C. M. Wenyon.*

SERGENT, Ed. & SERGENT, Et. La température des canaris sains ou paludéens. [**The Temperatures of Healthy and Malarial Canaries.**] *Arch. Inst. Pasteur d'Algérie.* 1946, Mar., v. 24, No. 1, 51–6, 4 figs.

A comparison of the temperature variations of normal canaries and those suffering from *P. relictum* infection has shown that there are no measurable differences in the two groups. The temperatures taken in the oesophagus, in the rectum and under the wing of normal birds show considerable variations, not only from day to day, but from one minute to another. It is evident that a malarial infection, even in its acute stage, is not associated with any departure from the normal range of temperature variations. The temperature of normal pigeons shows similar fluctuations. *C. M. Wenyon.*

THOMPSON, P. E. **Effects of Quinine on Saurian Malarial Parasites.** *J. Infect. Dis.* 1946, Mar.–Apr., v. 78, No. 2, 160–66, 3 figs.

For the experiments described in this paper the lizards *Sceloporus undulatus undulatus* and *Anolis carolinensis* were inoculated with *Plasmodium floridense*, and *S. undulatus cansobrinus* with *P. mexicanum*. In the first test two specimens of *S. u. undulatus* showing parasites in the blood were inoculated intra-abdominally with daily doses of quinine (140 mgm./kgm.). The treatment was started on the 18th day after inoculation. One of the lizards died after the 4th injection and the other after the 8th, as a result of the toxic action of the heavy doses of quinine. During the treatment there was no reduction in the number of parasites in the blood, but pronounced changes occurred in their morphology. These were the formation of large vacuoles in many of the parasites, irregularity in their outline, and loss of affinity for stains. Both asexual and sexual parasites were affected.

In a second experiment five strains of the parasite in *A. carolinensis* were studied in ten lizards, each strain in two lizards. One of each pair was treated and the other kept as control. The dose of quinine was reduced to 75 mgm./kgm. and this was administered every second day till 12 doses had been given. At the end of the course the parasites were difficult to find in the blood and a few days later it was impossible to detect them microscopically. During the course the parasites showed the degenerative changes noted above. The lizards were probably not cured, for parasites reappeared in one of them in 69 days. In a third experiment five *A. carolinensis* were inoculated with another strain of *P. floridense*. Three of the lizards were treated, the dosage being the same as in the second experiment, the first injection being given on the 39th day after inoculation. Six [? five, see Fig. 2] doses were given, with results similar to those in the second experiment. The effect of the drug on the parasites was still further tested by counting the number of merozoites in both treated and untreated lizards, commencing on the first day of treatment. In untreated lizards the merozoite number varied from $11{\cdot}2\pm0{\cdot}4$ to $14{\cdot}4\pm0{\cdot}8$, while in the treated lizards the number was reduced and varied from $7{\cdot}7\pm0{\cdot}4$ to $10{\cdot}0\pm0{\cdot}5$.

Similar experiments were carried out on *P. mexicanum*, which produces numerous exoerythrocytic forms. These occur in all the cells of the myeloid series, as well as in cells of the lympho-macrophage system. In the circulating blood about 70 per cent. of the parasites produce pigment. These are in the haemoglobin-containing erythrocytes, normoblasts and polychromatophile erythroblasts. The remaining 30 per cent. of the parasites which lack pigment occur in other cells which are devoid of haemoglobin. Two lizards were treated with 12 doses of quinine. The parasite levels remained high. This was accounted for by the fact that the drug acted only on those parasites which occurred in cells containing haemoglobin. The changes were similar to those seen in *P. floridense*. The parasites in the haemoglobin-free cells were not affected. Brain smears from treated lizards contained as many large asexual parasites as occurred in smears from untreated lizards.

The result of the experiments shows that the action of quinine on the malaria parasites of cold-blooded animals is similar to its known effect on parasites in various warm-blooded animals. *C. M. Wenyon.*

MANWELL, R. D. **Bat Malaria.** *Amer. J. Hyg.* 1946, Jan., v. 43, No. 1, 1–12, 1 text fig. & 16 figs. on 1 pl. [37 refs.]

The study described in this paper, in which the literature dealing with bat malaria is reviewed, was carried out on films from the blood and organs of two species of bat which are commonly infected with malaria parasites in New

Guinea. The bats are *Pteropus gouldi* and *Dobsonia moluccensis*. In most cases the only parasites found in the blood are pigmented gametocytes, of which those in *D. moluccensis* are larger than those in *P. gouldi*. The parasite in the former is recorded for the first time ; that in the latter is *Plasmodium pteropi* Breinl, 1911. In practically all instances the only forms present in the films were mature pigmented gametocytes, but in some of the blood films young pigmented forms were present in the red blood corpuscles. It is presumed that these are young gametocytes, as on no occasion was it possible to find pigmented schizonts. In a few films from *P. gouldi*, mature segmenting schizonts were discovered in fair numbers, but these were peculiar in that they were extracellular and devoid of pigment. It is suggested that they resemble certain exoerythrocytic schizonts of bird malaria parasites. If this be the case, it seems possible that the parasite of *P. gouldi* is more nearly related to species of *Haemoproteus*, and that the vector is likely to be found amongst the Nycteribiidae and Streblidae rather than amongst mosquitoes. *C. M. Wenyon.*

BLACKWATER FEVER.

Soeiro, A. N. Contribuição para o estudo da febre biliosa hemoglubinúrica. (Análise de 122 casos estudados no Hospital Central Miguel Bombarda, de Lourenço Marques.) [**Contribution to the Study of Blackwater Fever: Analysis of 122 Cases.**] *An. Inst. Med. Trop.* Lisbon. 1945, Dec., v. 2, 85–102, 1 fig. English summary.

McCance, R. A. & Black, D. A. K. ; Maegraith, B. & Havard, R. E. **Anoxia and Renal Function.** [Correspondence.] *Lancet.* 1946, Mar. 2, 362 & Aug. 10, 213–14. [16 refs.]

i. McCance and Black refer to a letter by Maegraith *et al.* [see this *Bulletin*, 1945, v. 42, 968] dealing with anoxia in relation to renal function. They are not convinced that all renal failures observed by them had the same pathological background.

They question why, if anoxia is the underlying cause of the functional renal failure, the syndrome should be encountered in uncompensated alkalosis. They discuss the difficulty in completely explaining the cause of renal failure in alkalosis, and suggest that it is not yet time to try to find a single explanation for the syndrome.

ii. In reply, Maegraith and Havard produce detailed arguments, based on their experiments and the experience of others, in support of their three main propositions regarding the term " renal anoxia " in which they had collected those renal syndromes having so much in common.

These propositions are : (1) that in these conditions, there is a reduction in the total renal blood flow, (2) that this is accompanied by a redistribution of the blood-flow within the kidney, and (3) that in consequence, there is anaemia and anoxia of the renal cortex. They admit that anuria in alkalosis is more difficult to explain ; but that, in all forms of the renal anoxia syndrome, it results primarily from failure of glomerular flow, and they offer a possible explanation of such failure in the case of alkalosis.

They recognize that there are lacunae in the evidence presented in their attempt to find a common factor in so widespread and complicated a syndrome

as renal anoxia, but suggest that their attempted simplification of the problem will make the necessary factual collection envisaged by Professor McCance " easier to give some direction to it ".

[This correspondence contains much concentrated physiological reasoning, which does not lend itself readily to abstracting. The letters should be consulted in the original.] *H. J. O'D. Burke-Gaffney.*

TRYPANOSOMIASIS.

Brazzaville [A. E. F.]: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1944 [Ceccaldi, J., Director]. 55–85. Maladie du sommeil. [**Sleeping Sickness.**]

In the introduction to his Annual Report for 1944, the Director of the Pasteur Institute of Brazzaville laments the fact that shortage of staff has compelled a disproportionate attention to administration and routine, at the expense of research. For five months of the year he and his " adjoint " were the only two qualified medical men on duty. Nevertheless the section of the Report devoted to sleeping sickness is somewhat longer than for some years past [this *Bulletin*, 1945, v. 42, 710; 1944, v. 41, 873; 1943, v. 40, 887; 1942, v. 39, 237; 1941, v. 38, 304].

New cases diagnosed and treated at the Institute during the year totalled 202 Africans and 1 European; 59 other Africans treated at the Institute had been diagnosed and had received initial treatment elsewhere, or were placed under treatment because of suspected sleeping sickness, without trypanosomes having been seen. Old cases under observation totalled 576 Africans and 9 Europeans.

New Cases.—A full history is given of the only new European case. This presents some unusual features. The patient was the senior administrative officer for the Bas-Chari department, with headquarters at Fort-Lamy, in the Chad region. He held this position from January 1939 to August 1942, during which period there were numerous opportunities of becoming infected. In fact, his servant, his dog and his cat all developed trypanosomiasis, but he suffered no more than a number of attacks of " malaria ". From August 1942 to April 1943, the patient was in South Africa, after which he was posted to Brazzaville, where the location of his house, and his movements, again created opportunities for becoming infected. He fell ill in May–June 1944, and in October trypanosomes were found in the blood, the cerebrospinal fluid showing 6 cells per cmm., and 39 mgm. albumin per 100 cc. He was treated with 5 injections of antrypol (maximum single dose 1·2 gm.) between October 16th and November 4th. On November 5th the temperature, which had settled within 24 hours of the first dose, shot up again, and trypanosomes were again seen [surprisingly] in the blood. The treatment was now changed to alternate injections of moranyl and tryparsamide, at weekly intervals, until November 21st. Temperature again subsided, but once more it shot up during treatment, and remained high, with cutaneous hyperaesthesia, and diarrhoea, before finally settling down, after a lumbar puncture on November 27th, which revealed 4 cells per cmm., and 30 mgm. albumin per 100 cc. The author ascribes the patient's sufferings during the later course of treatment to a meningism attributable to the arsenical medication, but the unfortunate patient seems also to have had to contend, during this period, with a quinine abscess in the buttock. The trypanosome infection is judged to have been acquired during the patient's posting to Brazzaville.

The 202 new African cases are tabulated according to the circumstances under which they were diagnosed (*i.e.* by mobile units, at various medical stations, on presenting the " passeport-sanitaire ", etc.), and also according to the stage of the disease. The analysis shows (as has so often been shown) that the percentage of early infections is always higher among cases diagnosed by mobile teams than among people who present themselves for treatment at fixed dispensaries. Thus, classifying the cases as those in (*a*) the lymphatico-blood stage, (*b*) the stage of meningeal reaction, and (*c*) the stage of meningo-encephalitis, the percentages discovered were as follows :—

	(*a*)	(*b*)	(*c*)
Mobile units	62%	4%	35%
Fixed dispensaries	14%	4%	82%

On the subject of treatments administered, and clinical progress, the Report goes into considerable detail, with numerous tabulations and long case-notes. Treatment of early (lymphatico-blood) cases were not entirely successful. Of 30 such cases followed up for 3 months to 1 year, only 22 were considered to have responded satisfactorily. Among 25 early cases treated by antrypol alone (6 weekly injections ; maximum dose 1·2 gm.) only 17 were regarded as successful ; 1 was " unsatisfactory ", in 3 the disease progressed, in 2 there were relapses, and there were 2 deaths. Toxic effects, attributed to the drug, in 2 cases, were loss of weight, albuminuria, and a generalized pruriginous erythema.

Late cases were treated by combined courses of antrypol and tryparsamide, or 270F (Orsanine) followed by tryparsamide. For results, the original Report, heavily laden with detail, should be consulted.

Old Cases.—Ample details are also given of the progress (generally satisfactory) of 9 European cases, whose earlier histories have been recounted in previous Annual Reports, and of 576 previously treated African cases. There were 27 deaths among the latter, 22 of which are ascribed to trypanosomiasis. All but 3 of these 22 had been diagnosed and treated in a late stage of the disease.

The problem of reinfection.—A case is described in which trypanosomes were again found in the blood six years after apparent cure. This is regarded as yet another instance of reinfection, a number of which, some as long as ten years after treatment, have been described and discussed in Annual Reports of recent years, from the Brazzaville Institute.

Trials with p-arsenosophenylbutyric acid.—Full details are given of these trials. The compound, here referred to as " para-arséno ", was introduced by EAGLE [see this *Bulletin*, 1945, v. 42, 15, 354, 970 ; 1946, v. 43, 1017], and it is this which has previously been designated as 70A [WEINMAN and FRANZ, *ibid.*, 1946, v. 43, 207]. A total of 70 patients were treated, by daily intravenous injections of 0·4 or (less commonly) 0·3 mgm. per kilo, for periods of 5 to 20 days. The majority of 20 patients treated in the stages of meningeal or cerebral involvement did not respond favourably. Combined treatment, 5 to 9 daily injections of " para-arséno " followed by 6 to 12 injections of tryparsamide, was administered to 5 patients in the later stages of infection. Although the cerebrospinal fluid picture improved, the effect was, on the whole, considered to be less favourable than after the customary course of 2 injections of orsanine followed by 10 of tryparsamide. As for the early, lymphatico-blood stage, 32 patients were treated by 11 to 20 daily injections of 0·4 mgm. per kilo. Trypanosomes reappeared in the blood in 5 cases, cerebral involvement developed in 3, further treatment had to be given because of apparently unfavourable immediate response in 6, and there was no follow-up in 1 case, so that only 17 (*i.e.* 53 per cent.) were provisionally cured, up to a

period of 7 months. The results in this stage of infection were therefore considered to be definitely inferior to those which would have been obtained with the established remedies. [The survey by EAGLE, this *Bulletin*, 1946, v. 43, 1017, includes consideration of these Brazzaville cases. He concludes that 90 per cent. of early cases may be cured by 12 to 14 daily injections of 0·5 mgm. per kilo.] *E. M. Lourie.*

GLASGOW, J. P. **The Seasonal Abundance of Blood-sucking Flies in a Grassed Woodland Area in Central Tanganyika.** *J. Animal Ecology.* 1946, May, v. 15, No. 1, 93–103, 2 figs.

These observations were carried out in conjunction with routine tsetse-fly rounds at Mpwapwa, Tanganyika, and were made in the hope of discovering "indicator species" which would point the way to an understanding of tsetse distribution and activity.

The following species were caught off a bait ox, and records were kept between July 1940 and December 1942:—Male and female *G. pallidipes* and female *Hippobosca longipennis*, *Phara speciosa*, *Tabanus atrimanus*, *T. insignis*, *T. taeniola*, *T. maculatissimus*, *Haematopota mactans*, *H. nobilis*, *Mesomyia fallax* and Pangoninae, a mixture of *Dorcalaemus compactus* (Austen), *Pangonius oldii* (Austen), *Nuceria neavei* (Austen) and two others, whose identity is uncertain.

The author gives a table and graphs showing the flight season and comparative densities of most of these species; some species are combined owing to possible errors in identification at the time. He states that there is little doubt that *Phara speciosa* and the Pangoninae have but one generation per year; *Haematopota nobilis* having a succession of generations, and *Mesomyia fallax* gives two populations each year (September and November). VANDERPLANK [this *Bulletin*, 1945, v. 42, 760] is quoted as saying that *T. taeniola* had the same flight season at Shinyanga in 1940. None of these species was suitable as an "indicator species", and the maximum numbers of adults do not normally occur in the same month in subsequent years, nor do the flight seasons coincide exactly. The possibilities of mechanical transmission of cattle trypanosomiasis are discussed. [Unfortunately the author does not state the time of day at which the fly-rounds were carried out, and whether they were carried out at the same time. The activity of many of these species is correlated with temperature and light intensity, and will vary considerably according to the prevailing weather.] *F. L. Vanderplank.*

JACKSON, C. H. N. **An Artificially Isolated Generation of Tsetse Flies (Diptera).** *Bull. Entom. Res.* 1946, Sept., v. 37, Pt. 2, 291–9, 2 figs.

The author wished to study what happens to *Glossina morsitans* in nature, particularly changes which occur with advancing age. He chose an area in which this species did not occur [though the reviewer may say from personal knowledge that the area was not grossly unsuitable to it]. He introduced pupae from elsewhere and allowed a very large number of flies to emerge during three consecutive days, after which the unhatched pupae were removed. It follows that any flies of this species which were subsequently caught must have travelled from this one spot, and have been of an age known within a narrow margin. The author has, in fact, carried out an experiment which adds precision to what has already been learned from wild flies, though it must be admitted that the environment was not strictly natural to this species.

After the liberation, flies were caught in a standardized way almost daily for sixty days. The wear and tear of wings and the distance from the point of release were recorded, and certain studies on weight, etc., were made. It was found that males showed evidence of not having fed up to the second or third day, and occasionally later. By the fourth day a considerable proportion showed evidence of having had a meal. In studying the fraying of the wings, standard categories were used, and the conclusion was reached, though there is much individual variation, that the mean age of a sample of flies can be estimated within about one day: there is a high coefficient of correlation between age and fraying. Studies of the amount of water, fat, etc., were also made. They are of value because they give a check to data collected from wild flies of unknown age.

From the recaptures it appears that the average distance travelled by the male is nearly four hundred yards in the first week, rising to nearly a thousand in the fourth. Many individuals travelled beyond a thousand yards and a few beyond two thousand. All the measures are taken, of course, direct from point to point.

So few females were recovered that little has been added to our knowledge of that sex.

Glossina swynnertoni occurred in small numbers in the area of the experiment and there is little doubt that some cross-breeding between it and the liberated *morsitans* must have occurred. But it is certain that there was a good deal of breeding among the *morsitans*, for a second generation of flies was captured. By studying the time which elapsed before the second generation appeared, the author concludes that the temperature to which insects and pupae had been exposed in this environment must have been rather close to those recorded in a Stevenson's screen. *P. A. Buxton.*

WILLIAMSON, J. & LOURIE, E. M. **Interference with the Trypanocidal Action of γ-(*p*-Arsenosophenyl) Butyric Acid by *p*-Aminobenzoic Acid.** *Ann. Trop. Med. & Parasit.* 1946, July, v. 40, No. 2, 255–64. [19 refs.]

γ-(*p*-arsenosophenyl) butyric acid, OAs $CH_2CH_2CH_2COOH$ was brought into prominence by EAGLE *et al.* [this *Bulletin*, 1945, v. 42, 15; 354]. The present authors confirmed that it acted on tryparsamide-resistant trypanosomes in mice as effectively as on the parent strain of *T. rhodesiense*. However, if the mice had just previously received 5 mgm. (per 20 gm.) or more of *p*-aminobenzoic acid by intramuscular injection, the trypanocidal action of an ED 90 dose of arsenosophenyl butyric acid was abolished. [The ED 90 is the dose which causes temporary or permanent disappearance of trypanosomes from the blood in 90 per cent. of mice.] *P*-aminobenzoic acid did not antagonize mapharside in this manner. The antagonistic effect was greatly diminished if the arsenosophenyl butyric acid was injected into the mice first and *p*-aminobenzoic acid was injected second. The same antagonistic effect could be demonstrated *in vitro* also, provided that the trypanosomes came into contact with *p*-aminobenzoic acid *before* they came into contact with arsenosophenyl butyric acid. Glutathione interferes with the trypanocidal action *in vivo* of arsenosophenyl butyric acid as much as it does with that of mapharside. It is concluded that *p*-aminobenzoic acid probably exerts its antagonistic effect by selectively limiting the admission of arsenosophenyl butyric acid into or on to the trypanosome cell, and that the underlying lethal mechanism for arsenical compounds (believed to depend on interaction with sulphydryl groups) is not involved.

F. Hawking.

CLAESSENS, H. Un mot sur la Propamidine iséthionate, utilisée à titre préventif, contre la trypanosomiase humaine. (Note préliminaire.) [**Propamidine Isethionate as a Prophylactic against Sleeping Sickness.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, Nos. 1/2, 7–12.

An investigation of the protective power of propamidine isethionate was carried out in two villages, of 77 and 82 inhabitants respectively, on the Kibombo-Kindu road, which is in a highly endemic sleeping sickness area of the Belgian Congo.

Nine infected persons were discovered in the two villages on March 7th, 1945. They were given full courses of treatment (detailed in abbreviated protocols case by case, at the end of the article), and all the other inhabitants were given an intramuscular injection of propamidine, 5 mgm. per kilo. body weight, in about 10 cc. water or physiological solution. Untoward temporary effects were (1) fever, (2) salivation and diminished sense of taste, and (3) a pruriginous papular eruption in a woman severely affected by macular leprosy.

Six months later, the location of the villages having been shifted meanwhile from the old to the new Kibombo-Kindu road, 131 of the combined population of 159 were re-examined (and re-injected with propamidine). Trypanosomes were discovered in 2 cases. One was judged to have become infected since the original injection of propamidine; no trypanosomes had been seen in lymph-gland juice 4 and 5 months subsequent to that injection, and, at the sixth month, when trypanosomes were seen in the gland juice, the cerebrospinal fluid was normal. The other case was one of the 9 who had been diagnosed at the beginning of the investigation, when she was given one injection of propamidine and seven of tryparsamide (3 gm. of the latter per injection).

On the basis of this [somewhat thin] evidence the author draws the conclusion that propamidine isethionate, used as he has described, does not confer protection, with absolute certainty, for a period of six months. *E. M. Lourie.*

EERAERTS, W. Etude et bayérisation d'un foyer actif et arsénicorésistant de trypanosomiase humaine. [**Investigation, and Prophylactic Treatment with Suramin, of an Endemic Area of Arsenic-Resistant Sleeping Sickness.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 233–43.

This is an interesting account of (1) the apparent development of arsenic-resistant sleeping sickness as the predominant type in an endemic area; (2) the methods of identifying cases of this type; (3) methods of treating such cases; and (4) eradication of the endemic focus by treating the entire population with Suramin (Antrypol, Bayer 205, Moranyl).

(1) *Development of arsenic-resistance.*—The work was carried out in the Feshi territory, Kwango District, Belgian Congo, about 7°S. latitude 18°E. longitude. The inhabitants are Basukus, a very primitive, improvident and ill-nourished people. The first case came to notice in 1937, and, by 1942, a total of 111 cases had been diagnosed in 5 villages of about 800 persons. In spite of repeated treatments, clearing of bush, displacement of villages, etc., the infection-rate in 1942 was still as high as 7 per cent.

Until 1939, the usual treatment was 1 injection of Moranyl, followed by 12 of Tryponarsyl. In 1940, Tryponarsyl alone was given. Since 1941, van Hoof's system has been adopted; this consists of a preliminary injection of 0·06 gm. Tryponarsyl (or Tryparsamide) per kilo. followed by an examination of the blood and lymph-gland juice 48 hours later. If trypanosomes are no longer found, treatment is by 12 injections of Tryponarsyl, but if they are still present the "cure arsénico-résistant" (see section 3 below) is instituted. Results have been as follows:—

	1937–9	1940	1941–2
Cases	16	14	66
Cured	15	10	23
Died of S.S.	1	1	1
Ocular troubles	1	1	1
Arsenic-resistance ...	0	3	42 (of whom 11 died)

It seems, then, that there has been a considerable development of arsenic resistance in the area, between 1937 and 1940, during which period Tryponarsyl was the main stand-by for treatment.

(2) *Identification of arsenic-resistance.*—The poor results in 1941–2, in spite of the adoption of van Hoof's system, led the investigator to question the reliability of this method. Among 16 new and 13 old cases subjected to the van Hoof test (persistence of trypanosomes 48 hours after 0·06 gm. Tryparsamide per kilo.) only 2, that is 7 per cent., gave a positive result. Nevertheless, all but four of the entire series (86 per cent.) eventually proved to be arsenic-resistant ; they were recognized as such by the fact that daily blood examinations revealed trypanosomes at varying periods from 3 to 33 days, in spite of courses of weekly Tryparsamide injections started on the 7th day since the test-dose.

Dr. van Hoof's comments, on being informed of these results, were that, whilst a positive result clearly demonstrates arsenic-resistance, a negative result does not necessarily exclude that condition, since the chemo-resistance is apparently of a degree which only just shows itself in the neighbourhood of the usual dosage for man. For itinerant practice, van Hoof therefore advises further blood examinations at about the 7th injection, say daily for 3 days immediately prior to that injection.

(3) *Methods of treating arsenic-resistant cases.*—The so-called Rodhain course is stated to be indubitably the most effective, but it is also extremely toxic. It should be given only under very careful conditions, and to subjects in good general condition. Of 34 patients so treated, only 16 supported the course well ; 5 died during the first week, 2 later in the course, and 2 within two months of the end of treatment. The course consists of :—

1st and 3rd day : Antrypol, 1 gm.
4th, 5th and 6th day : Tartar emetic, 0·07 gm., 0·09 gm., and 0·1 gm.
7th, 14th and 21st day : Tartar emetic, 0·1 gm., with Antrypol, 1 gm., in the same syringe.
followed by 10 injections of Tryparsamide.

Another course, apparently less toxic and quite effective, comprised 10 weekly injections of tartar emetic, 0·08 gm., together with Antrypol, 1 gm., in the same syringe in 10 cc. aqueous solution ; followed by 10 injections of Tryparsamide.

(4) *Eradication of the endemic focus.*—The entire population of 1,500 persons, was treated with Antrypol (or Bayer 205) in December 1942, and again 3 months later. On each occasion the dose for male adults was 1·5 gm., for females 1·25 gm., and for infants about 0·03–0·035 gm. per kilo. body weight.

Meticulous precautions were taken against toxic effects. Injections were given only between 5 and 10 a.m., on an empty stomach, after which the subject was required to rest in the shade for 2 hours. He was then seen again by the physician, before being allowed to go home, and he was exempted from work for 8 days. The urine was examined for albumin from 2 to 5 days after treatment, but was almost invariably normal. Toxic effects were negligible.

The procedure was regarded as entirely successful in clearing the endemic focus. Whilst 19 cases had been discovered at the time of the first injection (and given full courses of treatment), none was found 3 months later, although numerous cases were still to be found in the neighbouring sub-sector, across the River Nsaye. Later examinations, at intervals up to the end of 1945, failed to reveal a single case, except for one person in a typical late stage of infection, who must surely have been infected already, though not recognized as such, when she had received her 2 Antrypol injections about 15–18 months earlier.

The author is most enthusiastic about the value of prophylactic treatment with Suramin, which he regards as the prime method for dealing (by drug-treatment) with delimited endemic areas, particularly where infection is of the arsenic-resistant type. *E. M. Lourie.*

Morris, K. R. S. **The Control of Trypanosomiasis by Entomological Means.** *Bull. Entom. Res.* 1946, Sept. v. 37, Pt. 2, 201–50, 5 text figs., 3 maps & 12 figs. on 2 pls. [18 refs.]

The author gives a stimulating account of reclamation against tsetse in the Northern Territories of the Gold Coast. His base is entomological, but his scope includes trypanosomiasis in man and animals, and consideration of social and agricultural factors.

Morris writes of an important centre of sleeping sickness partly in British and partly in French territory. In 1938 the trypanosome rate in man was over 5 per cent., in an area of thirty thousand square miles inhabited by about 1,250,000 people. The particular district in which he worked, near Lawra, Northern Territory, Gold Coast, had a rate of 4–7 per cent. in a considerable area, and there were 1,100 admissions to hospital for trypanosomiasis in 1938. Parts of the district had become depopulated, apparently owing to this disease (though whether death or emigration was the more important is not known). Game and *G. morsitans* had spread into the land abandoned by man, and people were crowded on watersheds and ridges; here they were safe from tsetse, but the density of man and stock was producing serious erosion.

In clearing bush against fly (*G. palpalis* and *tachinoides*) the author distinguishes protective and eradicative work. Both, it is to be understood, are linear, along banks of water-courses. Protective clearing is often made where a road crosses a stream, and is carried up and down stream; of this work he has had long experience. He finds that a total clearing of 300 to 400 yards will reduce fly (both species) to about half what one would get in an uncleared area. If the clearing is lengthened to a mile it will still only be about 90 per cent. efficient, and even if it is three to five miles long an occasional fly will still reach the middle of it. Such flies could hardly have any importance as transmitters of human trypanosomiasis, but (owing to the much higher infection rate) they might transmit trypanosomes to cattle, and they might succeed in recolonizing an area which had been rendered fly-free. The effect on human trypanosomiasis of a large number of protective clearings is generally slow and not very great; for instance, in the Wa area a 70 per cent. reduction in cases followed after several years. [The author would, however, agree that it is most difficult to assess the results of this work. The population at risk or infected is not known. Admission to hospital, used as a measure of incidence, may be much affected by the popularity of one doctor. The disease in man is often chronic so that a lag is expected before the results of work are to be seen.]

Not satisfied with protective clearings, Morris turns to eradication. His general theory is that as *G. palpalis* and *tachinoides* are closely dependent (particularly in the dry season) on shelter in riverside fly belts, and as these

conditions depend on the growth of certain species of trees and bushes, he will take a strictly botanical line, and exterminate just these species. Moreover he hopes to achieve permanency or something near it, by starting at the top of a series of tributaries and working down, seeking to eliminate these particular trees and shrubs from a whole river system. [The reviewer, having seen tsetse reclamation in the northern parts of Nigeria and of the Gold Coast, is impressed by two points: the essential similarity in climate and vegetation; the similarity in methods employed, all based on a sound knowledge of ecology of fly, man and beast.]

This method has been applied to the Kamba valley. With its tributaries it has a total length of 250 miles, of which 105 miles were a dry-season breeding place of the two species of tsetse. There were 33,000 people in the area. Applying the method defined above, an enormous reduction in flies taken by fly boys was recorded, though neither *G. palpalis* nor *tachinoides* was completely eliminated. There was a very large reduction in cases of sleeping sickness at the local hospital; about 1,000 people returned and reoccupied farms on good riverine land: cattle were brought in, though they did not remain entirely free of trypanosomiasis.

The paper contains technical details on the labour and cost of digging up the stumps of certain species of trees which regenerate very freely. An appendix gives costs, but much too briefly. [One learns very little from "Control of *G. morsitans* £60." Tsetse workers ought to evolve a uniform scheme of costing their various sorts of work, and a uniform manner of presentation. It would be well to give figures in man-days as well as in currency. The point is commended to tsetse committees both in East and West Africa.]

Morris has travelled widely in West Africa, and evidently has close and valuable contact with French workers who are dealing with the same problem, indeed the same epidemic, in the Ivory Coast and other French territories. It is interesting to read his comparison of his own results with those of the French, obtained by mass diagnosis and treatment, and this is valuable even if the reader is left somewhat open-minded. *P. A. Buxton.*

ADLER, S. & BICHOWSKY, L. **The Action of Biotin Concentrate on *Trypanosoma cruzi*, *T. lewisi*, *Leishmania donovani* (Indian Strain) and *L. infantum* (Sudan Strain).** *Harefuah.* Jerusalem. 1946, Aug. 15, v. 31, No. 4. [In Hebrew 57–8. English summary 58.]

"It was found that biotin concentrate (S.M.A. Co.) has a marked inhibitory effect on the growth of *Trypanosoma cruzi*, *T. lewisi*, *Leishmania donovani*, and *L. infantum*. The concentrate was added to 5 ccs. medium (Locke-serum-agar) in quantities necessary to produce a required dilution and the medium was then inoculated with a measured quantity of flagellates (2×10^6 in the case of *Leishmania* and 1×10^6 in the case of the trypanosomes) and the number of flagellates per cc. medium was determined by counting in a haemocytometer after various intervals. There was no inhibitory action on *B. coli* or *S. aureus*. Typical experiments are shown in table I.

"On the strength of the above and similar experiments the possibility of biotin acting as an antibiotic for the above flagellates presented itself. Samples of crystalline biotin ester (not synthetic) obtained from S.M.A. Co. were variable in their action on the above flagellates—while with one sample 0·4γ per cc. medium completely inhibited the growth of *T. cruzi*, another sample showed only a third of this activity, and a third sample was completely inactive. The inactive samples were found to contain the full quantity of biotin as determined by biological assay on the growth of *Saccharomyces cerevisiae*. Synthetic

compounds, biotin (50 per cc. medium), biotin ester (2 per cc. medium), destiobiotin (10 per cc. medium), biotin amide (20 per cc.) had no inhibitory action on the growth of the above organisms. By adsorption methods (using kaolin, Fuller's earth and norit) it was also evident that there was no relationship between biotin content (as determined by assay on *Saccharomyces cerevisiae*) and inhibitory action on the flagellates.

"*Conclusion.*—Biotin concentrate contains a substance which inhibits the growth of *Trypanosoma cruzi*, *T. lewisi*, *Leishmania donovani* and *L. infantum*. The active substance is not biotin."

Guyane Française: Rapport sur le Fonctionnement Technique de l'Institut Pasteur de la Guyane Française et du Territoire de l'Inini pendant l'Année 1945 [Floch, H., Director]. (Publication No. 125. 1946. Cayenne.) pp. 83–5. Maladie de Chagas (ou Schizotrypanosomiase humaine). [**Chagas's Disease.**]

In 1944 investigations were undertaken to determine the numbers of laboratory-bred *R. pictipes*, *R. prolixus* and *T. rubrofasciata* infected by a single feed on guineapigs which had themselves been infected by strains of *T. cruzi* obtained from *Didelphys marsupialis*. The numbers examined were *R. prolixus* 80, *R. pictipes* 72, *T. rubrofasciata* 91, and metacyclic trypanosomes were found in 68, 65 and 29 respectively, or 85, 90 and 31 per cent.

E. Dias in 1940 demonstrated that *R. prolixus*, the chief vector in Venezuela, was more readily infected by a Venezuelan strain of *T. cruzi* than by strains from elsewhere and confirmed this analogously with *P. megistus* and *T. repetans* for Brazilian strains, and he suggested a series of xenodiagnostic tests as a means of recognizing the most dangerous of the vectors in places where Chagas's disease existed. According to this the above results would indicate that the French Guiana strains are specially adapted to *R. pictipes* and *R. prolixus*. Furthermore, that these strains are not well adapted to *T. rubrofasciata*. Nevertheless, in Cayenne, *T. rubrofasciata* is found heavily infected with a trypanosome which is not inoculable with success into laboratory animals; it is concluded that this trypanosome is, therefore, not *T. cruzi*, but is probably a trypanosome of bats, or, in Dias's opinion, possibly *T. conorrhini*.

It has been thought possible that cats become infected by eating infected mice, and Dias has reported finding the trypanosome in the blood 17 days after the meal, and the same may occur in dogs. Attempts have been made to infect three guineapigs by giving them bread containing infected Triatomidae, but so far without success. It may be, of course, that the cats when devouring the mice acquire small wounds of the buccal mucosa and infection may thus be by "submucous inoculation". *H. Harold Scott.*

Earle, K. V. **Penicillin in Chagas's Disease. With a Note on Chagas's Disease in Ecuador.** *J. Trop. Med. & Hyg.* 1946, Aug.–Sept., v. 49, No. 4, 74–6, 1 fig. [14 refs.]

There is here recorded the case of a man of 22 years, an Ecuadorean, with multiple infection by *T. cruzi*, *E. histolytica*, *P. vivax*, *Ascaris lumbricoides*, *Trichuris trichiura* and *Strongyloides stercoralis*. The signs and symptoms of the *T. cruzi* infection were typical except for the fact that palpebral and facial oedema, Romaña's sign, *followed* the findings of many trypanosomes in the blood. Mapharsen was given because, says the author, neither Bayer 205 nor tryparsamide was obtainable [nothing is said of the drug usually given with success in Chagas's disease, Bayer 7602], but was not effectual, so penicillin was tried—five injections each of 10,000 Oxford units at two-hour intervals on each of two days.

The trypanosomes disappeared after the 3rd injection and, except for severe headache, the symptoms cleared up. A second, similar, course of penicillin was, however, administered after an interval of three days. During the succeeding two months for which the patient has been under observation, trypanosomes have not been found and the patient "has felt perfectly well". The penicillin was administered intravenously because it was thought that the pain of intramuscular injections would scare the patient into defaulting.

Ecuador, says Dr. Vigors Earle, has not been named as a country in which Chagas's disease exists; *Triatoma dimidiata* is the only known intermediate host; other *Triatomas* are present, *T. carrione*, *T. venosa* and *T. coxo-rufa*, but these are not known to be vectors. An armadillo is common in rural districts but it has not been proved to harbour the trypanosome.

H. Harold Scott.

Ponce Caballero, L. Enfermedad de Chagas en Bolivia. Nota preliminar. [**Chagas's Disease in Bolivia.**] *Rev. Med. Chile.* 1946, May, v. 74, No. 5, 349–51.

The author carried out an investigation in Colcapirhua, a place with a population of 2,000, situated 10 kilometres east of Cochabamba. He visited five private houses, examined the blood of each of the inmates, by smear and thick drop, and by the xenodiagnostic method; also two cats and two dogs living in the house. None of the individuals showed signs of acute Chagas's disease. One person only, a man of 38 years, gave a positive result to xenodiagnostic tests; all the others, and the animals, proved negative.

He then examined the children of the local school. Several of them said that the bugs were abundant in their homes and that they were frequently bitten. Ten were tested by xenodiagnosis and six gave a positive result. One was an acute case, with palpebral oedema, enlarged preauricular gland, enlarged spleen and liver, fever, headache and malaise. In another case the xenodiagnostic test was negative but the blood gave a positive Machado-Guerreiro reaction. The other five had no subjective symptoms but they had enlarged livers and spleens and widespread adenitis; they owned that some time before they had suffered from swollen lids. These, therefore, were subacute and chronic cases. Direct examination of the blood was negative in all 10 and also in 7 others who were thus examined. The author concludes: "These cases show yet once again how rare it is to find *T. cruzi* in the blood; one knows that it multiplies in the tissues and that its presence in the blood is but transient."

H. Harold Scott.

LEISHMANIASIS.

Norman, A. P. **Latent Period in Kala-Azar.** [Correspondence.] *Lancet.* 1946, Sept. 21, 437–8.

The author, after referring to the literature, records a case of kala azar with a "presumptive latent period of two years."

The patient was a soldier of 26, who had served in E. Africa and the Middle East from April 1940 to December 1943, and thereafter for a few months in Italy.

In the summer of 1945, he noticed that "his belt seemed tight on exercise." In October, he was admitted to hospital with a history of one month's fever. There was a large tumour in the left hypochrondrium extending below the level of the umbilicus. All investigations, which were very full and included sternal

puncture for Leishman-Donovan bodies, proved negative. In November, laparotomy was performed, and the tumour proved to be a grossly enlarged spleen. Splenic puncture smear and cultures were negative for Leishman-Donovan bodies.

In December, as there was no improvement, the patient was treated for kala azar. He was given a course of stilbamidine, 0·075 gm., followed by 0·15 gm. daily, to a total dosage of 2·25 gm. Sweating decreased after a week, and the temperature dropped suddenly on the 13th day of treatment and remained low.

Later in December, a culture of marrow blood showed " distinct leptomonas forms of Leishman-Donovan bodies, fresh preparations showing characteristic motility."

Progress was slow, but excellent. In February 1946 a course of urea stilbamidine was given. In March the spleen was barely palpable and the anaemia was clearing up.

In April, the patient reported that he felt well, except for some numbness of the forehead, cheeks and lips.

Apart from the long latent period and the difficulty in diagnosis, the author notes the dangers of fifth nerve involvement which may follow the use of stilbamidine. *H. J. O'D. Burke-Gaffney.*

SARROUY, COMBE & CLAUDE. A propos d'un nouveau corps antimonié (2168 RP) dans le traitement du kala-azar infantile. (Note préliminaire.) [**Treatment of Infantile Kala Azar with a New Antimony Preparation. Preliminary Note.**] *Algérie Méd.* 1946, May–June, No. 3, 239–40, 1 chart.

The authors in studying the efficacy of a new product for the treatment of infantile kala azar, put at their disposal by Messrs. Specia and named 2168 R.P. (antimoniate of N methylglucamine) obtained spectacular results with their first patient.

This was a child of 5½, with a prolonged fever, and an enormous spleen and wasting. After full examination, numerous Leishman-Donovan bodies were found in a marrow smear.

The new drug, which is made up in a neutral and stable form, ready for injection, in 5 cc. ampoules, was given as follows, in daily doses intramuscularly:

" 1st day: 3 cc. (or 0·9 of 2168 R.P. or 0·255 of antimony) [presumably grammes]

2nd day and following days: 5 cc. (or 1·5 gm. of 2168 R.P. or 0·425 gm. of antimony).

In all, the child received 18 injections (or 26·4 gm. of 2168 R.P. or 7·48 gm. of antimony."

[These doses appear to be very high for a very debilitated child of 5½, stated to weigh only 16 kgm. See below.]

The temperature fell dramatically on the day after the first injection and remained low.

Early disappearance of the Leishman-Donovan bodies took place on the eighth day of treatment.

The splenomegaly resolved rapidly. The child became well and happy and no signs of intolerance to the drug occurred, other than a slightly subnormal temperature for 2½ days.

The authors consider that this result was strikingly superior to those commonly obtained with " Pentastib ", which in effective doses frequently produces signs of intolerance.

In mice, the new drug proved to be only half as toxic as Pentastib. The dose has not yet been fixed, and the authors are engaged in studying this problem, but they consider the present spectacular result worth noting.

[The doses of antimony quoted in the original paper appear to be considerably above the margins of safety commonly accepted. For example, NAPIER *et al.* (see this *Bulletin*, 1938, v. 35, 181) referring to the use of the antimony product, Bayer 561, in the treatment of kala-azar, give the total amount of antimony administered over 1 to 3 weeks as 0·96 to 1·79 gm., a maximum less than one-quarter of that quoted by the authors of this paper.]

H. J. O'D. Burke-Gaffney.

DURAND, P., BENMUSSA, S. & CARUANA, M. Traitement du kala-azar par un nouveau composé stibié : le 2.168 R.P. (premiers résultats). [**Treatment of Kala Azar with a New Antimonial, 2168 RP.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 24/25, 399–409.

The authors report on the results of treatment of the first six cases of kala azar with the new pentavalent antimonial 2168 PR, which is described as the antimoniate of N-methylglucamine, with the formula $SbO_3H,C_7H_{17}O_5N$. In mice, the drug was of low toxicity, the animals tolerating doses of more than 100 mgm. administered intravenously. The six cases of kala azar in which the drug was tried comprised five in children varying in age from 14 months to 14 years and one in an adult of 36 years. It was administered intramuscularly in a 30 per cent. solution, each 5 cc. containing about 1·5 gm. of the drug, representing about 0·5 gm. of antimony. The youngest child, of 14 months, was given two injections of 2 cc. followed by 15 of 5 cc. ; a child of 4½ years was given a course of 15 injections of 2·5 to 10 cc. followed a few weeks later by a second course of 12 injections of 10 cc. ; a child of 5½ years had two courses, one of 15 injections of 5 cc. and another of 10 injections of 5 cc., while another child of the same age was given a course of 20 injections of 5 cc. followed later by a second course of 13 injections of 10 cc. A boy 14 years of age had two courses of 15 injections of 10 cc. The adult was given two courses, the first being of 12 injections of 20 cc. As a rule the injections were given every two days, and where two courses were given, several weeks separated them.

In all cases the treatment was well tolerated and was followed by a general improvement in health and disappearance of leishmania from the bone marrow. The results obtained were so good that the authors have been encouraged to report their experience in spite of the fact that sufficient time has not elapsed to permit the conclusion that a permanent cure has been obtained. Three of the patients, one of whom had a history of three years' duration, had relapsed after treatment with diamidine. The new drug is rapidly excreted by the kidneys. In healthy subjects, all trace of antimony has disappeared from the urine in 24 hours. In cases of kala azar, excretion is less rapid, for after 36 hours traces of antimony could still be detected in the urine, but 12 hours later traces could no longer be found. *C. M. Wenyon.*

FEVERS OF THE TYPHUS GROUP.

NEUJEAN, G. Etudes sur les rickettsioses. III. Coloration et culture des rickettsias. [**Studies of the Rickettsial Diseases. III. Staining and Culture of the Rickettsiae.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 142–60, 20 figs.

The author gives further details of the technical methods employed by him in obtaining the extraordinary results mentioned in his previous paper [this

Bulletin, 1946, v. 43, 324]. He claims to have been the first to cultivate rickettsiae in the absence of living cells; his method is very simple. 5 cc. of blood is mixed with 1·0 cc. of " liquoïde Roche (1·0 per cent.) " and kept at room temperature for 24 hours; equal parts of this and Tyrode fluid are mixed and kept at room temperature. Smears of the mixture are examined at daily intervals. It is claimed that in cases of rickettsial disease the organisms can be found after 24 hours; when the infection occurs in latent form it takes several days to obtain an abundant growth.

The finding of rickettsiae in urinary sediment in cases of Congo typhus is again mentioned as being a method of early diagnosis; it is stated that the organisms persist " for months, if not longer "—" another proof, if this were needed, of the permanence of the infection."

The paper is illustrated by a series of 20 photomicrographs from which other workers can form their own opinions regarding the nature of the bodies described.

John W. D. Megaw.

NEUJEAN, G. & DOUCET, G. Etudes sur les rickettsioses. IV. Aspects cliniques du typhus congolais. [**Studies of the Rickettsial Diseases. IV. Clinical Aspects of Congo Typhus.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 161–95, 3 pls. & 21 charts.

The senior author has already described some results of his investigations into the typhus fevers of the Belgian Congo. In this paper further details are given of the clinical features of the disease, but these are stated in general terms. The clinical picture as described is in keeping with that of a fever of the typhus group. The laboratory procedures regarded as useful in diagnosis are :— (1) The Weil-Felix reaction, which, as stated in the earlier papers, has changed in type during the course of the investigation; at first high titre reactions with *Proteus OX19* strains were found, afterwards " cases with high titres have become rare; the *XK* type of agglutination, formerly feeble or negative, has become more frequent." (2) " The presence, even in traces, of albumin in the urine." (3) The finding of rickettsiae in urinary sediment is regarded as one of the best methods of diagnosis. *John W. D. Megaw.*

NEUJEAN, G. Etudes sur les rickettsioses. V. Typhus congolais et fièvre jaune. Valeur des réactions sérologiques. [**Studies of the Rickettsial Diseases. V. Congo Typhus and Yellow Fever. The Value of Serological Tests.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 196–8.

In view of the frequent occurrence of jaundice in cases of typhus fever in the Belgian Congo, and of the occurrence of black vomit and albuminuria in severe attacks, the author arranged for a series of Weil-Felix and mouse-protection (yellow fever) tests in 45 persons, all of whom were suffering from, or convalescent from, typhus fever.

In 11 sera of patients who had been vaccinated against yellow fever the mouse-protection tests were positive, in all the others the reaction was negative or doubtful.

The Weil-Felix reaction (*Proteus OX19*) was positive at titres ranging from 1–80 to 1–320 in 13 cases. The *OX2* reaction was positive at the same titres in 6 cases. The *OXK* titre was 1–80 in 26 cases and 1–40 in the rest. [These *OXK* titres can hardly be regarded as significant.]

The author concludes that the mouse-protection test for yellow fever retains its full significance when carried out on persons attacked by typhus fever.

John W. D. Megaw.

NEUJEAN, G. Etudes sur les rickettsioses. VI. Infections latentes et aigües décelées par l'inoculation au cobaye. [**Studies of the Rickettsial Diseases. VI. Latent and Acute Infections disclosed by Guineapig Inoculation.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 199–205, 12 charts.

By the blood-cultural method described in previous papers the author found that his healthy laboratory guineapigs were harbouring bodies indistinguishable from the rickettsiae already grown in blood cultures from patients infected with typhus fever. He mentions that a similar finding had been made in healthy human beings and in most of the animals examined in areas where cases of typhus fever were occurring.

In the present experiments, two guineapigs inoculated with blood from a typhus patient (*Proteus OX19* titre 1–320) had typical febrile reactions, and one of the animals had an orchitic reaction. Two guineapigs inoculated with blood from another typhus patient (*OXK* titre 1–80) had febrile and orchitic reactions.

Other guineapigs were inoculated, some with their own blood, some with blood of another guineapig, but although the inoculated blood in both sets of experiments had yielded positive cultures of rickettsia, the only response was a slight transient rise of temperature on the 11th day. The author concludes that the presence of a latent rickettsial infection does not interfere with the use of the animals for the diagnosis of active rickettsial infection.

John W. D. Megaw.

AMBERSON, J. M. **Typhus in Egypt during World War II.** *U.S. Nav. Med. Bull.* 1946, Sept., v. 46, No. 9, 1482–5.

In a brief paper of little more than three pages the author has summarized certain features of louse-borne typhus in Egypt from 1939 to the middle of 1945.

The disease is constantly endemic in Egypt; its "endemic level" is stated to have been 40 cases per 100,000 till 1941, when the "epidemic cycle" set in with an incidence of 55·5 per 100,000. The peak incidence was reached in 1943 when the index rose to 229·24; in this year the case-fatality rate was 20·2 per cent. In 1944 the incidence was 105·9 and the death rate also fell to 16·85. The figures for 1945 were incomplete at the time of writing, but up to June the fatality rate had fallen further, to 11·59, so that the epidemic cycle was "on the downward grade."

A list is given of the signs, symptoms, and complications, observed in 196 cases "gathered at random"; a curious feature of the list is that no mention is made of the occurrence of haemorrhages or thromboses.

The only reference to murine typhus is in the statement that "cities along the Suez Canal have the murine form as well." *John W. D. Megaw.*

MUSGRAVE, A. J. **Tests on Clothing impregnated with DDT as an Anti-Louse Measure.** *Bull. Entom. Res.* 1946, May, v. 37, Pt. 1, 43–56. [10 refs.]

As a method of testing the toxicity, to lice, of treated cloth, pieces were clipped off impregnated garments and put, with lice, into gauze-bottomed louse-breeding boxes worn daily on the leg. Observations of mortality among the lice were made after 1, 2 and 4 days, and the fabrics assessed as:—

Very effective if there was complete kill in 1 day;
Effective " " " 2 days;
Moderately effective if there was complete kill in 4 days;
Slightly effective " " 50 per cent. or more in 4 days;
Not effective " " less than 50 per cent. kill in 4 days.

Tests were made with various garments (mainly shirts of Angola material), and the results were related to chemical estimations of the DDT content. The garments were distributed as follows :—

Biological assessment	Chemical analysis (per cent. DDT wt/wt)				
	Less than 0·04	0·04 –0·08	0·09 –0·19	0·2 –0·5	More than 0·5
Not effective	8	2	1	0	0
Slightly effective ...	2	2	1	0	0
Moderately effective ...	0	1	1	0	0
Effective	0	0	3	3	1
Very effective ...	0	0	0	1	2

In another type of test, the lice were allowed to crawl on treated Angola shirting for various periods and then transferred to clean tape. It was concluded that one hour's exposure to 1·75 per cent. impregnated fabric was lethal to all lice in a few hours, while there was a high subsequent mortality after three hours' exposure to 0·1 per cent. DDT. Adult lice were observed to show early signs of poisoning clearly after four to six hours on 0·1 per cent. fabric and after two hours on 1·75 per cent. fabric at 30°C.

Miscellaneous tests showed that DDT is fairly persistent at high temperatures and also that impregnated garments transfer their insecticidal power to paper, or unimpregnated garments, kept in contact with them. It is suggested that the chief loss of insecticidal power is due to loss of impregnated fibres from the surface of the cloth. *J. R. Busvine.*

Oz, T. V. Typhus profilaktisinde Kudüs mektebi. **[Typhus Immunization : Kudus Method.]** *Türkische Ztschr. f. Hyg. u. Exper. Biol.* Ankara. 1943, v. 3, No. 1, 117–20. German summary 121.

At the Kudus Institute in Jerusalem a vaccine of rickettsiae of a murine strain was prepared from male guineapigs. The animals were killed when the scrotal reaction was positive, at the height of fever ; the tunica vaginalis was triturated and distributed into 5 Erlenmeyer flasks each containing 4·5 cc. Tyrode solution and 0·5 cc. guineapig serum. This mixture was held at 30°–32°C. for 5 days, then centrifuged, and the sediment mixed with 10 cc. physiological saline containing 0·1 per cent. formaldehyde. The suspension was held in the ice-box for 15 days, and then tested for sterility, harmlessness to guineapigs and antigenicity.

Inoculation of this vaccine in man gives immunity for 6 months to 2 years [the number of injections, and the dose, are not stated in the German summary]. *Charles Wilcocks.*

Levine, H. D. **Pathologic Study of Thirty-One Cases of Scrub Typhus Fever with especial reference to the Cardiovascular System.** *Amer. Heart. J.* 1946, Mar., v. 31, No. 3, 314–28, 10 figs. [17 refs.]

This is a clear and succinct description of the naked-eye and microscopic changes observed in a post-mortem study of 31 cases of scrub typhus during the year 1944. More than half of the deaths occurred between the 12th and 15th days : the extreme range was 6 to 24 days.

Details of all the chief naked-eye changes are given in tabular form ; the microscopic findings are illustrated by 10 photomicrographs which show

pericardial infiltration, myocardial necrosis, endothelial proliferation and hyperplasia, pneumonic infiltration, and haemorrhage with focal necrosis in the adrenal cortex.

The findings are summed up by the author in the words :—" The changes described here are quite similar to those found in European (epidemic) typhus."

A few of the chief findings are as follows :—In 27 cases the heart was pale, soft, flabby or slightly friable. In 22 cases there were subpericardial petechial haemorrhages ; in only one was there a macroscopic haemorrhage into the heart muscle. Microscopic changes were found in the heart in 25 cases ; in 13 of these the muscle fibres were intact, in the other 12 there were minor degrees of degeneration. Perivascular exudation was a pronounced feature ; the endothelium of the small vessels in the region of these showed proliferation in many cases.

There were subpleural haemorrhages in 7 cases. The lower lobes of the lungs were usually consolidated, either uniformly or in patches ; the middle and upper lobes were seldom affected. Microscopically, some degree of inflammatory reaction was found in the lungs in every case but one ; the reaction consisted of intra-alveolar and interstitial exudation of lymphocytes, plasma cells, and large mononuclear cells ; in 7 cases the exudate contained polymorphonuclears, which were regarded as being due to secondary infection. In heavily congested areas the alveolar spaces contained numerous red blood cells.

The liver was enlarged in 8 cases. Subcapsular haemorrhages were seen in three. Microscopical findings were :—congestion of the central veins and hepatic sinusoids with degenerative changes in the central cells of the lobules, in 18 cases.

Haemorrhages were seen in the mucosa of the renal pelvis in 7 cases. In 22 there was congestion of the renal blood vessels. Multiple small haemorrhages were seen among the straight tubules in 16 cases. An inflammatory exudate was seen in the renal parenchyma in 15 cases. Occasionally there was extravasation of blood into the renal cortex.

The leptomeninges were congested in 8 cases. Petechial haemorrhages were seen in the cut surface of the brain in 11. In 15 cases the meninges were infiltrated with a diffuse or focal monocellular exudate.

In 23 cases there was oedema of the ankles or accumulation of fluid in one of the serous spaces.

The author states that " from the available evidence it is likely, therefore, that patients who survive scrub typhus fever ultimately show no residua cardiac damage."

John W. D. Megaw.

BENGTSON, Ida A. **A Serological Study of 37 Cases of Tsutsugamushi Disease (Scrub Typhus) occurring in Burma and the Philippine Islands.** *Pub. Health Rep.* Wash. 1946, June 14, v. 61, No. 24, 887–94, 1 fig.

The author has already shown that sera of persons or animals infected with known strains of tsutsugamushi rickettsiae, when tested by the complement-fixation reaction, gave much higher titres with antigens of the homologous strains than with those of heterologous strains [this *Bulletin*, 1946, v. 43, 551].

In the present study 37 sera were tested :—15 from Burma, and two lots of 7 and 15, respectively, from the Philippine Islands. In the comparative tests three strains of antigen were used :—the Karp (K), from New Guinea ; the Gilliam (G), from Assam ; and the Seerangayee (S), from the Federated Malay States. The technique employed was that originated by the author. The Weil-Felix test (*OXK*) was also carried out in each case.

Several samples of sera from each of the 15 patients in Burma, taken at different stages of the illness, were tested.

A few examples of the remarkable variations observed in the responses are given below; these have been taken from the Table in the paper, which gives details of the results obtained in each test. The examples given here do not illustrate all the types of response that were observed; as the author states "all possible combinations of K, G, and S, are represented in the results of the tests on the sera of the 37 cases."

	Day of disease	*OXK* Titre	Complement-Fixation Titre			Type of reaction
			Karp	Gilliam	Seeran-gayee	
Burma series	35	100	2,048	8	2,048	KS
	12	Neg.	256	32	2,048	S
	29	100	64	4,096	512	G
	20	800	8,192	1,024	65,536	KS
Philippine 1st series	32	320	8,192	8,192	4,096	KGS
	2nd month	20	16	64	64	KGS
	6th month	20	4	512	Neg.	G
Philippine 2nd series	16	1,280	16,384	32,768	32,768	KGS
	11	20	256	8	4	K

The author points out that "by the use of the K and G antigens antibodies would have been detected in all the sera tested."

In general, considerably higher and more persistent titres were obtained with the complement-fixation test than with the Weil-Felix.

The results do not show any clear differentiation of serological types such as had been suspected to exist. *John W. D. Megaw.*

Bengtson, Ida A. **Complement Fixation in Tsutsugamushi Disease (Scrub Typhus).** *Pub. Health Rep.* Wash. 1946, June 14, v. 61, No. 24, 895–900.

This paper was scheduled for publication on February 11th, 1944, but was withheld because of the subject.

The author describes the preparation of an antigen from the Karp strain of tsutsugamushi rickettsiae. The original strain was received, in the form of frozen specimens of infected chick embryos, from Dr. Lewthwaite of the Federated Malay States. After some preliminary difficulties the strain was found to grow readily in yolk-sac cultures, and the antigen was prepared by a modification of a method found suitable for other rickettsiae of the typhus group.

The antigenic titres obtained were 1–4 to 1–8; these were lower than those of epidemic and endemic rickettsiae, which were 1–16 to 1–64.

Sera of seven guineapigs convalescent from infection with tsutsugamushi rickettsiae yielded complement-fixation titres of 1–16 to 1–64 with the antigen, which was found to be specific as shown by the occurrence of completely negative reactions when it was used in tests of sera which had given strongly positive reactions against their respective homologous antigens in the cases of the following diseases:—epidemic typhus, endemic typhus, undulant fever, Rocky Mountain spotted fever, tularaemia, typhoid fever and syphilis.

In tests of sera of six patients convalescent from tsutsugamushi disease, completely positive reactions were obtained in five cases at titres ranging from 1–32 to 1–2,048; in the sixth case a partial reaction at 1–16 was obtained. In four of the fully-reacting sera, check tests were carried out with antigens of epidemic typhus, endemic typhus, Rocky Mountain spotted fever, and Q fever;

in every case the responses were completely negative. All the above six sera reacted strongly with the Weil-Felix (*OXK*) test, at titres ranging from 1–1,280 to 1–20,480. *John W. D. Megaw.*

AMERICAN J. HYG. 1946, July, v. 44, No. 1, 1–5. [29 refs.] **Q Fever: a Foreword. Introduction to a Series of Papers dealing with Q Fever.**

This is an introductory preface to a remarkable series of papers dealing with the investigation of a number of outbreaks of Q fever which originated in the Mediterranean area during the early months of 1945, and with a single case which occurred in Panama in August 1945.

All the papers dealt with in this and the following 11 abstracts appear in the same number of the *American Journal of Hygiene*; these papers contain not only detailed descriptions of the investigations carried out by their authors but also numerous references to previous work on the disease, which hitherto had been known to occur in Queensland, Australia, where it was first discovered in 1935, and in the U.S.A. where a very few cases had been detected.

The first event leading up to the present investigations was information received in London from Major-General Biggam, late R.A.M.C. of the Army Medical Staff, and members of his staff, to the effect that outbreaks of "atypical pneumonia" had occurred in various bodies of British troops in the Mediterranean area, that these were anomalous in being confined to certain units in which the attack rates were very high, and that they were not associated with the prevalence of other respiratory illnesses.

Soon afterwards it was found that similar outbreaks had occurred among American troops.

The first systematic investigation of an outbreak was in February 1945; it dealt with the men of a British Parachute Battalion, stationed in Italy, who were convalescent from attacks of the disease; their infection had apparently been contracted in Athens, where they had been stationed before their arrival in Italy.

From the latter part of February till the end of April of the same year, four similar outbreaks among American troops stationed near Florence and Bologna were studied.

In February 1945, Dr. J. Caminopetros, of the Pasteur Institute of Greece, informed Major Zarafonetis of the U.S.A. Typhus Commission that an outbreak, called by the German physicians "Balkan grippe", had occurred in Athens during the winter of 1943–1944, and that the infecting agent had been transmitted by him to guineapigs. From a sample of blood from one of the infected guineapigs *Rickettsia burneti* was later isolated at the Respiratory Diseases Laboratory in the U.S.A.

In August 1945, *R. burneti* was isolated in Panama from a patient whose disease had been diagnosed as "atypical pneumonia".

The broad results of the investigations are that a disease previously classified under various names, such as atypical pneumonia and Balkan grippe, is Q fever, and that all the known strains of the causal agent, *R. burneti*, are closely related to each other in their immunological properties, though certain antigenic differences have been found to occur. *John W. D. Megaw.*

ROBBINS, F. C. & RAGAN, C. A. **Q Fever in the Mediterranean Area: Report of its Occurrence in Allied Troops. I. Clinical Features of the Disease.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 6–22, 6 figs. [21 refs.]

Eight outbreaks of a disease resembling primary atypical pneumonia are said to have occurred in Italy, Greece, and Corsica, during the cold-season

months of 1944–45. Five of these were investigated, and in all of them specific antibodies against *R. burneti* were demonstrated; the organism itself was isolated in three of the outbreaks.

The present clinical description is based on observation of the following groups of cases:—

(1) In a U.S.A. Infantry Company stationed near Florence (53 cases);
(2) In a U.S.A. Infantry Battalion in the same region (267 cases);
(3) In the 6th Battalion Parachute Regiment (British) near Rome, but quite recently stationed in Athens (40 cases);
(4) In a U.S.A. Military Laboratory at Naples where work was being done on the rickettsia of the disease (20 cases).

The general clinical picture was:—The onset was sudden; commonly with a chilly feeling, sweats, malaise, weakness, frontal headache, and anorexia. Aches in the muscles and pain in the chest sometimes occurred.

About half of the patients had retro-orbital pain; this was seldom severe. A slight cough often occurred about the 5th or 6th day, sometimes with a little blood-stained sputum.

The fever curve showed great fluctuations, especially when salicylates were given. The fever lasted 4–15 days; termination was by lysis.

In most cases a few crepitant râles, diminished breath sounds, or dullness on percussion, could be detected in localized areas by the 4th or 5th day.

In the British outbreak, splenomegaly and generalized adenopathy were reported to have occurred in about half of the cases; these signs were not present in the other outbreaks.

By X-ray examination patchy areas of consolidation were seen in most of the cases, usually in the lower lobes of the lung.

The attacks varied greatly in severity, but there were no deaths.

Blood cultures remained sterile, and all the usual serological tests, including the Weil-Felix reaction, gave negative results.

R. burneti was isolated 16 times in 20 attempts, by inoculating guineapigs with blood taken on the 2nd to the 8th day of the disease. A positive result was obtained in four cases in which there was no evidence of consolidation of the lung.

Sulphonamides and penicillin were useless in the cases in which they were tried.

Notes of six cases, illustrated by temperature charts, are given.

John W. D. Megaw.

ROBBINS, F. C., GAULD, R. L. & WARNER, F. B. **Q Fever in the Mediterranean Area: Report of its Occurrence in Allied Troops. II. Epidemiology.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 23–50, 8 figs. [33 refs.]

Five of the outbreaks of Q fever in the Mediterranean area were investigated from the point of view of epidemiology.

In the first of these, 53 cases of "primary atypical pneumonia" had been diagnosed during February and March 1945, among 156 soldiers who were occupying a requisitioned farmhouse and its ancillary buildings near Florence. The ground floor of the farm house was used for storing grain and sheltering livestock, which included cattle, horses, pigs, sheep, chickens, cats, and dogs. Rats and mice were numerous, and large numbers of pigeons nested in the various buildings.

The incidence was 44–48 per cent. among the men living in attics and hay barns, and 23 per cent. among those living in the first-floor rooms.

R. burneti was isolated from three patients, and the complement-fixation test was positive in sera of 48 out of 53 convalescents.

There was no evidence of person-to-person transmission. The probable incubation period was 14 to 26 days.

In the largest of the outbreaks described, 269 cases occurred in a unit of about 900 men, between April 7 and 29.

The unit was in a camp close to a farmhouse near Florence. A course of intensive training was being carried out ; this included cinema demonstrations in the loft of a barn containing old dusty hay, on which the men sat. Numerous pigeons nested in holes in the walls, and in the nests larval ticks (*Argas reflexus*) and rat fleas (*X. cheopis*) were found.

On the floor of the loft large numbers of tiny mites of various species were found.

The first case appeared 18 days after the unit entered the area. The incubation period was estimated as being 17–23 days. The outbreak was explosive ; 63 per cent. of the cases occurred in the six days, April 10–15.

The various diagnoses made in hospital were :—Atypical pneumonia, pneumonitis, or primary pneumonia, in 188 cases ; no final diagnosis, in 28 cases ; fever of undetermined origin, in 24 cases ; common respiratory disease, in 20 cases ; sinusitis in three cases ; hepatitis and malaria in two cases each, influenza and meningitis, in one case each.

A complete epidemiological enquiry was impracticable. An insect vector was considered unlikely because very few of the men complained of bites. Inhalation of dust infected with dried excreta of rats, mice, or pigeons, or of insects such as ticks, must be considered.

All the other outbreaks were of the same general type ; there was usually an association with animals such as pigeons, rats, mice, and cattle ; also with dust on floors or in hay and straw. It is suggested that mites may have been inhaled with the dust, as is reported in Ceylon, where a kind of asthma is said to be caused by inhaled mites [this *Bulletin*, 1945, v. 42, 73].

The sporadic occurrence of the disease in Italy is mentioned ; sera from 49 isolated cases, diagnosed as atypical pneumonia, in April 1945, were tested, and 29 of these gave positive reactions with the complement-fixation test. The patients were stationed in Caserta, near Naples. *John W. D. Megaw.*

Robbins, F. C., Rustigian, R., Snyder, M. J. & Smadel, J. E. **Q Fever in the Mediterranean Area : Report of its Occurrence in Allied Troops. III. The Etiological Agent.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 51–63, 1 fig. [20 refs.]

The authors isolated 16 strains of *R. burneti* from 20 patients by injecting 3–5 cc. of freshly drawn blood into each of two guineapigs. In the successful attempts one or both of the animals became febrile after an incubation period of 5-13 days. In the later passages through guineapigs the incubation period ranged from 4 to 8 days.

Apart from fever and enlarged spleen, the guineapigs showed no sign of infection ; no rickettsiae could be detected in smears of the spleen, tunica, or other organs. Guineapigs inoculated with yolk-sac material heavily infected with the organisms became febrile within 24 hours and died in 5–9 days with haemorrhagic pneumonia. Innumerable rickettsiae were found in smears of the spleen and tunica.

Swiss white mice did not react to inoculation ; white rats and hamsters were doubtfully susceptible to suspensions of infected guineapig spleen, but died within 5 days when inoculated with heavy doses of infected yolk-sac suspension ; smears of the spleen and tunica showed innumerable rickettsiae.

The organisms grew readily in yolk sacs of chick embryos ; ten strains were established from suspensions of spleen of infected guineapigs, and another from

blood and serum of a human patient. In early passages the embryos died in 8–10 days; after further passages death occurred in 4–6 days.

Infected blood or spleen suspensions of guineapigs were still infective after passage through Mandler porcelain candles, No. 7, 8 and 9.

The complement fixation test was carried out on the lines described by Bengtson; details of the technique are given.

Titres over 1–10 were found to be specific; two of 13 sera from cases of primary atypical pneumonia reacted at 1–10, and two syphilitic sera gave a partial reaction at this titre. In psittacosis, murine typhus, and epidemic typhus the reactions were negative.

A rickettsia-agglutination test was employed to a small extent.

The results of the complement-fixation test were of special interest. When one strain of *R. burneti* isolated in Italy, the "Henzerling strain", was used, the reaction became positive between the 7th and the 13th day in every case of Q fever; the maximum titre was reached about the 21st day; when the American strain (Dyer) was used, the reaction was always negative. So also, serum of the Panama Q fever patient was negative with the American strain, though it reacted at a titre of 1–160 with the Henzerling strain. Sera of a group of guineapigs convalescent from infection were tested, using the same two strains as antigens; up to the 40th day the reaction with the American strain was feeble or negative, with the Henzerling strain it was positive, but between the 40th and 76th day the reactions with both strains became positive at about the same titres.

In further comparative tests five different strains were used, *viz.*, the above two, an Australian strain, and two other strains isolated in Italy; the Henzerling and Australian strains gave similar results, but the other three strains gave much weaker reactions. The differences were found to be quantitative, disappearing when larger quantities of the three feeble antigens were used.

The results suggested that the rickettsiae had two antigenic fractions and that all strains contained considerable quantities of the Henzerling-type antigen, which, therefore, is likely to be generally applicable for use in the test, whereas the American and some other antigens may be of restricted value.

The Henzerling antigen was found to retain its complement-fixing potency after heating to 70°C. for half-an-hour.

An interesting finding was that when sera were tested by the rickettsia-agglutination reaction the titres of those that had reacted weakly with the American strain and strongly with the Henzerling strain in the complement-fixation test showed no difference; they agglutinated both types of organisms at similar titres. The authors point out that in the agglutination test the dilutions used are 1–5 or 1–10, whereas in the fixation test they are 1–80 to 1–160.

John W. D. Megaw.

ROBBINS, F. C. & RUSTIGIAN, R. **Q Fever in the Mediterranean Area: Report of its Occurrence in Allied Troops. IV. A Laboratory Outbreak.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 64–71, 1 fig. [10 refs.]

During June, July and August, 1945, 20 proved cases of Q fever occurred among 107 persons employed in a Medical General Laboratory of the U.S.A. Army in Italy. Every one of the six workers in the Virus Section was attacked; three of the four persons working in the adjoining Adjutant's Office were attacked, and six of the 14 workers in the Medical Arts Section, which was separated from the Virus Section by a short internal passage. Among the remaining 83 persons working in the building there were only four cases.

All but one of the patients had either been working with *R. burneti*, or had some association with the Virus Section. Inhalation of air infected with the organism appeared to be the most likely mode of infection.

The outbreak was most closely correlated with work on yolk-sac cultures; infection in guineapigs had been maintained for 2½ months previously, without mishap.

The virulence of the infection had probably been increased by passage through guineapigs, and the high concentration of rickettsiae in chick embryos may have greatly increased the risk of infection. *John W. D. Megaw.*

FEINSTEIN, M., YESNER, R. & MARKS, J. L. **Epidemics of Q Fever among Troops returning from Italy in the Spring of 1945. I. Clinical Aspects of the Epidemic at Camp Patrick Henry, Virginia.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 72–87, 9 figs. [20 refs.]

In May 1945, 7,500 U.S.A. troops were disembarked at a harbour in Virginia after a nine-day voyage from Naples. Up to 36 hours after their arrival, 62 of the men were admitted to hospital with acute fever. It was found that 55 of the patients belonged to the 717th Bomb Squadron, whose total strength was 379. Attacks continued to occur till 15 days after arrival, and by this time 143 cases had occurred, so that 38 per cent. of the members of the squadron were affected.

In 90 per cent. of the cases pneumonic lesions were found by X-ray examination and the disease was identified as Q fever by serological tests.

By a systematic X-ray examination of all the men of the squadron, 31 symptomless cases were found.

The early cases were rather severe; many of the later attacks were mild or symptomless.

The symptoms of the 128 patients who had positive X-ray findings were as follows; the figures in brackets refer to percentage incidence.

The onset was gradual (69·5) or sudden (30·5). Other features were:—headache (75); feverishness (73·4); malaise (50); weakness (43·7); chilliness (40·6); backache (24·2); cough (62·5); chest pain, not severe (43·9); nasal discharge (23·4); expectoration (26·6); sore throat (14·1); anorexia (36·7); constipation (33·6); nausea (15·6); and pain with stiffness of the neck suggesting the possibility of meningitis (24).

The physical signs observed were:—Pharyngeal injection (78·9); nasal congestion (36·7); cervical adenopathy (31·3); fine crepitant râles (41·4); moist râles (14·1); dullness on percussion (32·8).

The maximum temperature was:—102°F. or over (37·5); 100 to 101·8° (35·2); 99 to 99·8° (10·9); and 98·8° or less (16·4).

The duration of the illness was:—more than 7 days (8·5); 5–7 days (32·8); 2–4 days (47·6); 1 day (7·0); and indefinite (3·9).

The severity of the illness was classified:—Acutely ill (14·1); moderately ill (29·7); and mildly ill (56·3). The course of the disease was always benign, no patient was prostrated even while the temperature was high. Only three patients had blood-stained sputum early in convalescence.

A detailed analysis is given of the distribution and location of the lesions shown by X-ray examination. Eight clear photographs are reproduced. Dividing the lung region into six equal zones—three on each side—the lesions were more frequent in the lower and middle zones than in the upper. Only one zone was involved in 44·5 per cent. of the cases, but two, three, four or more zones were affected in some cases. The lesions were classified as:—"bronchitic", when situated at the roots of the lungs; "peribronchial", when they were round the bronchi as in primary atypical pneumonia; and "alveolar", when in the outer third of the lung field in the form of "ground-glass patches", but there was often a combination of two or all three of these

types. The lung lesions disappeared on the average in 10·8 days, but this duration is said probably to be an underestimate.

The routine blood examination yielded little information, except that in early convalescence a slight degree of leucocytosis was often observed.

In the early stages the disease could not be differentiated, except by X-ray examination, from many other acute febrile diseases. The lung lesions differed from those of primary atypical pneumonia in their distribution and character ; the infrequency of respiratory symptoms and physical signs were also helpful points. *John W. D. Megaw.*

AMERICAN J. HYG. 1946, July, v. 44, No. 1, 88–102, 3 figs. [10 refs.] **Epidemics of Q Fever among Troops returning from Italy in the Spring of 1945. II. Epidemiological Studies.** By the Commission on Acute Respiratory Diseases [DINGLE, J. H., Director].

This is a study, by the Commission of Acute Respiratory Diseases, of the epidemiological aspects of the outbreak dealt with in the preceding paper, and of other outbreaks of Q fever.

From the 717th Bomb Squadron which left the Grottaglie Air Base near Taranto in Italy on May 13th, 1945, and arrived in the U.S.A. on May 24th, 144 cases were analysed. Between the 18th and 24th of May, 56 cases occurred and further attacks continued to occur in gradually diminishing numbers till the 6th of June.

It was found that four other Bomb Squadrons which had been stationed at Grottaglie at the same time had a similar experience, so that about one-third of the group of 1,638 men were attacked. In 50 per cent. of the cases the onset fell within a period of six days ; and allowing for an incubation period ranging from 14 to 26 days it appeared that infection had occurred about the 6th to the 8th of May.

Every possible source of infection was carefully considered, but the great explosive outbreak remained an enigma. The authors were inclined to think that the men had been exposed to the bite of some insect during the time that they were engaged in cleaning the camp area before leaving the base ; at this time they were sleeping in the open. Mites or other minute arthropods, whose bites escaped notice, might perhaps have been the vectors ; mosquitoes, ticks, and sandflies were not present in large numbers, otherwise their presence would certainly have been detected by the men.

In spite of the large number of opportunities of person-to-person transmission during and after the sea voyage, no case of the disease occurred among contacts coming from uninfected localities. *John W. D. Megaw.*

AMERICAN J. HYG. 1946, July, v. 44, No. 1, 103–9. [13 refs.] **Epidemics of Q Fever among Troops returning from Italy in the Spring of 1945. III. Etiological Studies.** By the Commission on Acute Respiratory Diseases [DINGLE, J. H., Director].

This is an account of an investigation into the aetiology of the outbreak described in the two preceding papers. The causal organism was not isolated, but only four patients with mild attacks at the end of the outbreak were investigated by animal inoculation with blood taken on the 2nd or 3rd day of the illness.

Sera of 112 patients were tested by the complement-fixation reaction during the acute and convalescent stages of their illness ; of these 36 showed no rise in titre ; 26 showed a two-fold rise, and 50 a four-fold or greater rise.

An interesting finding was that positive reactions occurred in 13 per cent. of the 228 men of the 717th Squadron who appeared to have escaped infection.

John W. D. Megaw.

AMERICAN J. HYG. 1946, July, v. 44, No. 1, 110–22, 2 figs. [29 refs.]

Identification and Characteristics of the Balkan Grippe Strain of *Rickettsia burneti*. By the Commission on Acute Respiratory Diseases [DINGLE, J. H., Director].

In May 1945 a sample of blood from a guineapig infected with a fever-inducing agent was received from Dr. J. Caminopetros of Athens. The source of the infection was a patient suffering from "Balkan grippe", and the strain has been maintained by guineapig passage for 13 months.

The strain was found to cause fever lasting 3–4 days in guineapigs, with an incubation period of 4–9 days; and to grow well in chick yolk sacs, producing very large numbers of rickettsia-like bodies many of which were in clumps. The clumps were most numerous in the allantoic fluid, where some of them were so large as to be visible to the naked eye.

In infected guineapigs there was neither enlargement of the spleen nor scrotal reaction; occasionally there was some increase in the pleural and peritoneal exudate, but no organisms could be detected in smears of the fluid.

Mice, inoculated intraperitoneally with infected yolk-sac material, died or were moribund about eight days later; there was splenic enlargement, and numerous rickettsiae were found in smears of the spleen and other organs, also in pleural and peritoneal exudates. The organisms appeared as minute pleomorphic rods and as cell inclusions made up of masses of rickettsia-like bodies.

Sera of guineapigs inoculated with the strain, and of patients suffering from laboratory infection caused by the same strain, gave positive complement-fixation reactions when Australian or Italian strains of *R. burneti* were used as antigens.

The strain was then used in carrying out a series of rickettsia-agglutination tests on sera of human patients, and of guineapigs inoculated with the strain. The results were compared with those obtained by complement-fixation tests of the same sera, using the Australian and one of the Italian strains as antigens. The results of the tests were in general agreement.

The antigens used in the rickettsia-agglutination tests were prepared by a method based on the procedures employed by Craigie and Topping in the preparation of epidemic-typhus vaccine. Details are given of the technique that was adopted.

A critical test was made to find the range of error inherent in the agglutination test. The same sample of serum was tested on 39 different occasions and the titres observed were 1–64 or 1–128 in all the tests except one, in which the titre was 1–256; the same antigen was used throughout the tests.

Six different samples of the antigen were prepared in the same way, and were used in comparative tests on each of 145 sera from Q fever patients. In each test any two of the six samples were compared. The error was seldom more than a two-fold difference in the titres; in five there was a four-fold variation, but in only one of these was the lower titre less than the diagnostic figure of 1–8.

In a laboratory outbreak caused by the Balkan grippe strain, repeated rickettsia-agglutination tests were carried out; all the 16 patients reacted at titres of 1–8 or higher; 11 reacted at 1–128 or more. None of the unaffected members of the staff reacted at a titre of 1–4.

The test appeared to be strictly specific; the titre was less than 1–4 in every one of 89 control hospital patients; among these there were 33 cases of primary atypical pneumonia in which 77 tests were made; the other control patients

suffered from a great variety of illnesses. Similar negative results were obtained in 362 sera of healthy persons.

Among the Q fever patients the reaction was always negative till the 10th day; in tests made between the 10th and 15th days it became positive in 17 and 25 per cent., respectively, of two groups of patients; between the 22nd and 31st days the corresponding percentages were 76 and 90.

On 56 sera the agglutination test was compared with a complement-fixation test in which the Italian strain of antigen was used; a significant complement-fixation titre of 1–20 was obtained in 25 of these sera, and among the 25 positives there were four that gave a titre of less than 1–4 with the agglutination test. Conversely 29 of the sera gave titres of 1–8 or more with the agglutination test, and among these positives there were four in which the fixation titre was less than 1–10. *John W. D. Megaw.*

American J. Hyg. 1946, July, v. 44, No. 1, 123–57, 20 figs. [22 refs.]
A Laboratory Outbreak of Q Fever caused by the Balkan Grippe Strain of *Rickettsia burneti*. By the Commission on Acute Respiratory Diseases [Dingle, J. H., Director].

In the Fort Bragg Laboratory, North Carolina, 15 of the 49 workers, and one visitor, became infected with the Balkan grippe type of *R. burneti* between July 30 and December 22, 1945, in spite of increasingly strict precautions. The mode of infection was believed to be inhalation of droplets of infected yolk-sac material which entered the air in the course of processing.

The outbreak is described in minute detail; the paper is illustrated by 20 figures, which include 7 clinical charts and 12 X-ray photographs.

[The symptomatology as described corresponded in general with that of the naturally-occurring outbreaks already discussed in the previous papers, but the average severity of the attacks was greater, so it seems likely that the virulence of the infection had been increased by repeated passage through guineapigs and yolk-sac cultures; the infecting dose may also have been excessive.]

Experimental work on the strain was started on May 3, 1945, but work on the large-scale preparation of antigen from yolk-sac cultures commenced about the middle of July.

Six workers among a group of eight who handled infected eggs were attacked, and the two who escaped had worn masks. All the attacks occurred in conditions compatible with the inhalation of infected droplets or droplet nuclei. In one case the incubation period was almost certainly 16 days. Contact with infected animals had also occurred in some cases, but not in all.

The fever lasted 6–17 days. There were few respiratory symptoms, but 14 of the patients had lung lesions demonstrable by X-ray examination.

In six cases attempts were made to isolate rickettsiae by guineapig inoculation with blood taken in the acute stage; in four of these positive results were obtained; and in one case, in which three such attempts had failed, pleural fluid withdrawn on the 9th day caused a typical infection.

Fuller details are given of the rickettsia-agglutination tests referred to in the preceding paper. The maximum titres were usually reached in the 5th and 6th weeks, when most of the patients reacted in titres of 1–64 to 1–256, though in two mild cases no agglutinins were detected till the 5th week, and the highest titre in one of these was 1–16.

Sera of seven patients were repeatedly tested against the three usual strains of *Proteus*; no rise in titre occurred in any case, and no titre higher than 1–80 was observed.

Only one patient gave a positive reaction with the cold agglutinin test; the negative response to this test helps to differentiate the disease from primary atypical pneumonia.

No constant change occurred in the blood picture ; in late convalescence the neutrophiles in four cases were less than 40 per cent. of the total leucocytes.

It is stated that 42 other cases of laboratory infection with Q fever have been recorded in Australia, the U.S.A., and Italy. *John W. D. Megaw.*

CHENEY, G. & GEIB, W. A. **The Identification of Q Fever in Panama.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 158–72, 6 figs. [12 refs.]

This case of Q fever in Panama was not discovered by accident. The author thought that some of the cases of atypical pneumonia in the canal zone might be caused by rickettsiae, and accordingly carried out guineapig inoculations in selected cases.

In August 1945, a patient who had not been absent from the area for three months was attacked by acute fever. On the third day of the illness each of two guineapigs was inoculated intraperitoneally with 5 cc. of his blood ; eight days later both animals became febrile, and from them a strain of rickettsia was isolated and passed through nine successive pairs of guineapigs. The only gross change in the infected guineapigs was enlargement of the spleen, but in smears made from the tunica vaginalis intracellular and extracellular rickettsiae were found, and there were cytoplasmic inclusion bodies in the large serosal cells.

Glycerinated tissue of an infected guineapig was sent to the National Institute of Health, Bethesda, where the strain was passed through guineapigs which, after recovery, were found immune to the American strain of Q fever rickettsiae ; conversely guineapigs convalescent from the American strain of infection were immune to the Panama strain.

The clinical features of the patient's illness were entirely consistent with the diagnosis of Q fever with lung involvement. On the 40th day the complement-fixation test was positive at a titre of 1–512.

Complement-fixation tests for the fevers of the typhus group were negative during the acute stage of the disease, but on the 23rd day a positive reaction for Rocky Mountain spotted fever, at a titre of 1–20, was observed.

The Weil-Felix reaction to the three usual strains of *Proteus* was found to be negative on seven occasions up to the 29th day, but on the 45th day the *OX2* titre was 1–80 and the *OX19* titre was 1–160.

No evidence was found which threw any light on the source or mode of transmission of the infection. *John W. D. Megaw.*

TOPPING, N. H., SHEPARD, C. C. & HUEBNER, R. J. **Q Fever : an Immunological Comparison of Strains.** *Amer. J. Hyg.* 1946, July, v. 44, No. 1, 173–82, 1 fig. [10 refs.]

Details are given of experimental studies of the immunological relationship between the following six strains of *R. burneti* :—(1) an Australian strain, (2) an American strain, (3) the Balkan grippe strain, (4) a strain isolated in the Fort Bragg laboratory outbreak, (5) the Panama strain, and (6) the Henzerling Italian strain.

All the strains grew readily in yolk-sac culture and were similar in their morphology. Each strain killed one or more of the lots of chick embryos that were inoculated, in the same average time of five days ; but the average day of death of all the lots inoculated with each strain varied from 3·9 in the case of the Fort Bragg strain to 5·4 for the Panama strain.

Complete cross immunity between five of the strains was demonstrated by guineapig inoculation ; the Australian strain could not be tested because it could not be established in guineapigs during the time occupied by experimental work.

The average duration of the fever in non-immune guineapigs inoculated with the strains ranged from 3·08 days with the Fort Bragg strain to 4·8 days with the Panama strain.

The antigens, studied by the Bengtson complement-fixation technique, showed great variations in their sensitivity when employed in tests of the sera of infected guineapigs; the Italian and Balkan-grippe strains of antigen were consistently sensitive and gave high-titre responses with sera of guineapigs convalescent from infection with all the strains except the Australian, which, as stated above, did not lend itself to the experiment. Antigens of the American, Fort Bragg, and Panama strains were much less sensitive, and were therefore regarded as unlikely to give good results when used in the complement-fixation tests.

The details of the experiments are fully recorded; they cannot readily be summarized. *John W. D. Megaw.*

YELLOW FEVER.

Orenstein, A. J. **The History of Yellow Fever and its Present Status.** *Pub. Health.* Johannesburg. 1946, Sept., v. 10, No. 8, 13–25, 2 charts.

Smithburn, K. C. & Haddow, A. J. **Isolation of Yellow Fever Virus from African Mosquitoes.** *Amer. J. Trop. Med.* 1946, May, v. 26, No. 3, 261–71. [20 refs.]

This important paper records the isolation of yellow fever virus from *Aëdes simpsoni* caught in Western Uganda in a very sparsely populated region where effective mass immunization of the human population had been carried out eleven months previously; and also from mosquitoes caught in the uninhabited Semliki Forest.

Bwamba, a small county in Western Uganda, has been the site of investigations since 1937, when a high incidence of yellow fever immunity was found among the local inhabitants. In this region *Aëdes aegypti* occurs, but its behaviour is unusual, for it breeds in tree holes, and the adults are rarely taken whilst biting man: it is scarce in inhabited areas and in huts. There was an outbreak of yellow fever in this locality in 1941 and the virus was isolated from two lots of *Aëdes simpsoni*. Subsequent immunity surveys showed that the highest incidence occurred in the regions bordering the main forest, and a high percentage of forest monkeys were found to be immune.

Intensive collection of mosquitoes has been carried on since 1942; the insects were sent to Entebbe for inoculation into laboratory animals (rhesus monkeys and mice). Yellow fever virus was isolated from *Aëdes simpsoni* caught at Bundinyama in 1942. Subsequently 48,924 mosquitoes, collected in various parts of the Semliki Forest up to the end of 1943, were examined and three unknown viruses were isolated, but no more cases of yellow fever were found. In April 1944, a mixed lot of *Aëdes* mosquitoes from Mongiro, a dense primeval rain forest, was found to contain yellow fever virus; Rift Valley fever virus was isolated from a group of *Eretmopodites* and from another group of *Aëdes tarsalis*. The batch of *Aëdes* containing yellow fever virus included 80 insects belonging to 12 different species, *Aëdes aegypti* and *Aëdes simpsoni* not being represented. After April 1944, yellow fever virus was not found, although a total of 35,525 Bwamba mosquitoes were sent to Entebbe for inoculation into animals.

In their discussion the authors consider that the results indicate the presence of an extra-human cycle of yellow fever in the Semliki Forest, and that monkeys

are the principal mammalian hosts. The results of immunity tests in monkeys show no significant difference in the immunity rate between species which spend much of their day time on the ground and those which only rarely come down, and then only for short periods. This may be explained by the presence of a vector active in the forest canopy between sunset and sunrise, when both arboreal and terrestrial monkeys are in the trees. *Aëdes africanus* fulfils this requirement, being scarce at ground level but common 50 to 60 feet above ground, and it is constantly present in the canopy.

It is suggested that the human host may become infected when monkeys leave the forests and invade plantations in search of food. In Bwamba, the redtail monkey, *Cercopithecus nictitans mpangae* Matschie, is a notorious raider, and these animals are not only susceptible to yellow fever, but many immune individuals have been found in nature. *E. Hindle.*

MAHAFFY, A. F., SMITHBURN, K. C. & HUGHES, T. P. **The Distribution of Immunity to Yellow Fever in Central and East Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Aug., v. 40, No. 1, 57–82, 10 figs. [10 refs.]

The adaptation of the Yellow fever virus to mouse brain by Theiler in 1930 was followed by the development by SAWYER and LLOYD of a simple intraperitoneal mouse protection test for measuring neutralizing antibody for the virus in blood serum. In 1931, the International Health Division of the Rockefeller Foundation began an investigation of the geographical distribution of immunity to yellow fever in man as measured by this test. As a result of a number of surveys in North, East, West and South Africa, the approximate boundaries of the continental zone of immunity to yellow fever were determined.

In 1937, the Yellow Fever Research Institute was established in Entebbe, Uganda, under the directorship of Dr. A. F. Mahaffy, to carry out more intensive studies in yellow fever in Central and East Africa. The previous surveys have been extended in order to delimit more accurately the zone where yellow fever has occurred. The same basic intraperitoneal mouse protection test has been used as in the original surveys, but the strength of virus used has gradually been reduced from 20 per cent. to 1 per cent. in order to increase the sensitivity of the test. The results obtained from 1937 to 1943 are contained in this report. These findings have been of great value in defining the endemic areas of yellow fever in Africa, which have become so important with the great increase of air traffic.

The survey showed that yellow fever has occurred recently in the Belgian Congo, Uganda, the Anglo-Egyptian Sudan, Eritrea, Somalia, Kenya and Northern Rhodesia. Positive tests were obtained with sera from as far east as the Red Sea coast of Eritrea and as far south as Balovale in Northern Rhodesia; Tanganyika Territory and Zanzibar have been free of recent infection. Abyssinia has not been adequately studied.

The endemic zone in Africa is now considered to lie within the following boundaries :—a line running from the mouth of the Senegal river, along that river east to 15°N. parallel of latitude and thence eastward along that parallel to the eastern boundary of Anglo-Egyptian Sudan, thence northwards along the north-west boundary of Eritrea to the Red Sea Coast. Thence southward along the eastern coast of Africa to the southern boundary of the Protectorate of Kenya, thence westward along that boundary and the southern boundary of Kenya Colony to its junction with the southern boundary of Uganda Protectorate, thence along this and the eastern border of the Belgian Congo to 10°S. parallel of latitude, thence westward along that parallel to the west coast of Africa and thence northward along the west coast to the mouth of the Senegal river,

including the islands in the Gulf of Guinea. The Port of Massawa is excluded. [In *Epidem. Information Bull.* UNRRA, 1946, v. 2, 772, it is stated that an area 10 kilometres in radius from the centre of the town of Asmara is also excluded. The Barotze Province and the Balovale District in Kaonde-Lunda Province in N. Rhodesia are also included in the African endemic yellow fever area.]

Clinical cases of yellow fever have never been recognized in Eritrea, Western Somalia, central Kenya or Northern Rhodesia, and only recently in the Anglo-Egyptian Sudan. The value and specificity of the mouse protection test was brought out by the very large epidemic in the Nuba Mountains in the Anglo-Egyptian Sudan in 1940. Immune bodies for yellow fever had been detected in sera from this region some years previously, but it had been impossible to detect any patients with a disease resembling yellow fever as it is generally known. Similar difficulties were encountered in the present survey in Bwamba county in Uganda. It was only after the protection tests demonstrated the existence of the disease, in a restricted area within recent months, that the authors were successful in diagnosing active clinical cases. " The explanation of this lies, in part at least, in the fact that a high percentage of cases in Africans are mild, and mild yellow fever cannot be diagnosed clinically. These are points which are still by no means universally appreciated. Severe and fatal cases of yellow fever, presenting the classical symptoms of the disease, do occur in Africa, but they are so infrequent that, under the conditions which prevail there, the fact that they have not been seen and recognized does not constitute a sound basis on which to declare an area free of the infection."

[This article should be read in detail by those in the Colonial Medical Service in Africa in order that they may be familiar with the areas in which yellow fever has occurred.] *F. O. MacCallum.*

Epidemiological Information Bull. (UNRRA Health Division). Washington, D.C. 1946, Aug. 15, v. 2, No. 15. 618–32. **Dakar Yellow Fever Vaccine. An Experiment to determine the Immunizing Powers of Yellow Fever Vaccine produced by the Pasteur Institute at Dakar.**

Under article XI of the International Sanitary Convention for Aerial Navigation, 1944, UNRRA is obliged to " lay down standards with which yellow fever vaccine shall conform ", and international certificates of inoculation against yellow fever issued in accordance with article XI of the Convention are valid only when the vaccine and the method of inoculation have been approved by UNRRA. The experiment to determine the immunizing power of the neurotropic brain vaccine made by the Pasteur Institute at Dakar was devised by an expert group of the Quarantine Commission.

The efficacy of the Dakar vaccine was compared with two lots of chick embryo vaccine containing the attenuated 17D strain of yellow fever virus. The latter type of vaccine is that which has been used in South America and Africa since 1939 and has proved an effective immunizing agent in the field.

A sample of the batch of Dakar vaccine contained 10,422 mouse lethal doses per cc. and a sample of the 17D vaccine from U.S.A. contained 49,506 lethal doses per cc. [The interval between inoculation and onset of symptoms or death in the mice is of course much shorter after injection of the Dakar vaccine.]

Six hundred and thirty young adult French soldiers from a single regiment, none of whom had been out of France, were divided into three groups of 210 each. One group, A, received the Dakar vaccine only, a second group, B, the Dakar vaccine mixed with smallpox vaccine, and the third group, C, the 17D vaccine.

Before injection into Group A the Dakar dried vaccine was ground in a sterile mortar mixed with a special solution of gum arabic prepared in ampoules at the Pasteur Institute, Dakar. It was inoculated by means of scarification in the left deltoid region. Light scarification of 0·5 cm. in length were made in two groups of two. Owing to the mixture of gum arabic with the vaccine, the scarifications after being left to dry for five minutes were found to be covered with a very thin film of gum which ensured the protection of the scarifications.

For the second group, the mouse brain vaccine was prepared as for the first group in gum arabic, and the smallpox vaccine then incorporated.

For the third group the 17D vaccine was prepared as directed and inoculated subcutaneously.

There were no really significant reactions but a higher proportion of the men in groups A and B had headache, stiffness, ocular and periorbital pains, on the 6th or 7th days.

The men were bled 36–37 days after inoculation. The sera were separated on the following days, each serum divided into two parts, given a code number and one part sent to Dakar and one to Washington to be tested for immune bodies. The original intracerebral mouse protection test of Theiler was used at Dakar. The standard adult mouse intraperitoneal test was used in U.S.A. A comparison of the results showed discrepancies in 92 cases. There was sufficient sera from 86 of these for a further test to be made at Rio de Janeiro by the intracerebral method.

In group A, men who received the French neurotropic mouse brain vaccine alone, neutralizing antibodies were found in 186 of 192 sera (96·88 per cent.) tested at Dakar, and in 190 of 190 (100·0 per cent.) tested in U.S.A. The mouse brain vaccine plus smallpox vaccine produced 97·47 per cent. positive when tested at Dakar and 98·96 per cent. positive in U.S.A. There was thus no doubt about the immunizing potency of the batch of neurotropic mouse brain vaccine made at Dakar and applied by scarification either alone or in combination with smallpox vaccine.

On the other hand, in the group of men who received the 17D strain vaccine, the percentage of positive sera was only 55–60 per cent. as measured by the intracerebral protection test, and 97–100 per cent. as measured by the intraperitoneal test. The intracerebral tests at Rio seemed slightly more sensitive in detecting antibody in this group of sera than the tests at Dakar. [Though the group of men who received the 17D vaccine from U.S.A. was very small, the percentage of positive sera was very similar to that of the groups receiving 17D vaccine from London.]

[These results are very interesting for a number of reasons. The first vaccine recommended, after the discovery of the virus in 1928, consisted of an emulsion of ground infected monkey liver rendered non-infectious by various chemical inactivating reagents. It was found, however, that such inactive virus was not capable of producing active immunity. The next stage was use of active mouse-adapted neurotropic yellow fever virus and human convalescent serum. However, this method was limited by the very large amounts of immune serum which were necessary for large-scale immunization. LAIGRET and other French workers used a mouse-passage neurotropic virus without immune serum, but as THEILER and WHITMAN pointed out on the basis of experimental evidence, this procedure seemed highly dangerous. This was subsequently borne out by several French workers who described a considerable number of cases of encephalitis after use of their vaccine.

Since that time it has become increasingly evident that mice may carry latent virus and other infections in their brain which may be pathogenic for man. For these reasons an attempt was made by the workers of the Rockefeller Foundation to obtain an attenuated but living strain which would produce

satisfactory immunity but little or no reaction. Such an attenuated strain, 17D, was obtained after many unsuccessful attempts in tissue cultures, and vaccine has been made on a large scale since 1939 in U.S.A., South America and England, by inoculation of developing chick embryos with this strain of virus.

Its immunizing capacity has been amply tested in the field in South America and demonstrable neutralizing antibodies have been found in 96 per cent. of a group of individuals four years after inoculation. The present test also showed that 97–100 per cent. of the inoculated individuals had neutralizing antibody in their blood. The main drawback to the use of this vaccine is its marked instability at temperatures above 5°C., especially when the virus is in solution. It was interesting to note that although the 17D vaccine contained nearly five times as many mouse lethal doses of virus as the Dakar vaccine, it produced demonstrable immune bodies in the serum, as measured by the intracerebral protection test, in a much smaller percentage of individuals.

The potency of the dried Dakar vaccine is said to persist for two months after leaving the laboratory, provided it is kept in an ice-box. The vaccine may be transported at " ordinary " temperatures, if for not more than a few days. Its stability is thus about the same as the dried 17D vaccine. Though the Dakar vaccine produces a greater degree of immunity as measured by serum antibody, the fact that the 17D vaccine does produce serological neutralizing antibody in the sera of 97–100 per cent. of recipients with no chance of extraneous infection (as far as known at present) or encephalitis, the latter vaccine appears to be the more suitable for use. There is no doubt that it would be much more satisfactory to have an inactivated virus, and it is possible that with some of the newer methods of concentrating virus and exposure to a process such as ultra-violet radiation, a stable, innocuous and satisfactory antigen may be achieved.] *F. O. MacCullum.*

Brazzaville [A. E. F.] : Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1944 [Ceccaldi, J., Director]. 49–53. Fièvre jaune. [**Yellow Fever.**]

The Pasteur Institute at Brazzaville continued to use the yellow fever vaccine containing 17D virus from the Rockefeller Foundation in 1944/45. Batches of vaccine were found to have retained their potency after two to three years' storage at temperatures of 5°C. to 10°C.

A reaction, on the sixth day after injection, was observed in only one of the 710 individuals who received the yellow fever vaccine.

Mouse protection tests on sera from various regions showed positive sera from Libreville, the youngest positive patient being a child of 11 years ; from Donghila, where the youngest positive was 10 years, and 7 of 14 adults and 5 of 10 children were positive ; and from N'Djole, where the youngest was 13 years old.

A small experiment with 15 mice suggested that penicillin might have slight virucidal action on neurotropic yellow fever virus *in vitro* [see also Linhares, this *Bulletin*, 1945, v. 42, 373.] *F. O. MacCallum.*

PLAGUE.

DAVIS, D. H. S. **A Plague Survey of Ngamiland, Bechuanaland Protectorate, during the Epidemic of 1944–45.** *South African Med. J.* 1946, Aug. 24 & Sept. 14, v. 20, Nos. 16 & 17, 462–7; 511–15, 1 fig.

Ngamiland, the region around Lake Ngami, is included within the Bechuanaland Protectorate. Directly or indirectly, by sylvatic rodent or human outbreak, this vast area includes a consideration of Angola, South West Africa, the Kalahari and the Rhodesias. Plague had only been enzootic for some fifteen years in Ngamiland and the Bechuanaland Government had dispersed "its Rodent Staff when the 1935 scare died down." Human infection in the Kalahari made its appearance in October 1944, took the Government completely by surprise, but was, with the help of the Government of Southern Rhodesia, vigorously dealt with. The occasion was used to make a survey of the rodent and flea fauna and "to trace the course and history of the epizootic in the rodent populations which had culminated in the epidemic," an epidemic "which was destined to be the largest outbreak in Southern Africa on record." Table 1 of recorded human infection gives a total of 304 cases with 156 deaths. A sketch map shows the itinerary followed in this difficult territory and the difficulties are well and vividly described in the text. An excellent account is given of the sylvatic plague cycle and these articles are well worth consulting by any one interested in, or advising on, the history and course of plague epidemics in backward regions. Briefly speaking the permanent reservoir of plague in South Africa is the gerbil (*Tatera* spp.) and this rodent species suffers notably from what is considered to be epizootic plague of multi-focal origin. Even more important than the gerbil is the multi-mammate mouse (*Mastomys*), for it is the villain of the piece, because it is semi-domestic or, as the case may be, semisylvatic. This mouse is very fertile, does not provide much shelter for itself, makes much use of the burrows and nests of the gerbils and other rodents. picks up the infective gerbil flea, *X. eridos*, brings it to human habitations and so transfers plague to the domestic rodent whose flea, *X. brasiliensis*, is, with the gerbil flea, an efficient vector to man. In the present epidemic, most of the cases were of bubonic plague with a certain proportion of septicaemic and a few which were pneumonic. An outbreak of this type, especially when utilized for the collection of information, provides valuable data for what is called "central strategy", the strategy which is careful to avoid futile activity.

W. F. Harvey.

i. PERRY, J. S. **The Reproduction of the Wild Brown Rat** (*Rattus norvegicus* **Erxleben).** Reprinted from *Proc. Zool. Soc. London.* 1945, v. 115, Pts. I & II, 19–46, 7 figs. [17 refs.]

ii. LAURIE, E. M. O. **The Reproduction of the House-Mouse** (*Mus. musculus*) **living in different Environments.** *Proc. Roy. Soc.* Ser. B. 1946, Aug. 7, v. 133, No. 872, 248–81, 6 figs. [39 refs.]

These papers are of interest because they give solid demographic facts about common rodents. They are a valuable contribution to the quantitative ecology of plague, or other rodent-borne disease, and they may help workers in the tropics to produce similar work for other animals. The two papers are written by men with training in the physiology of reproduction, and they set a new standard of work. They are here noticed briefly and generally.

i. In the first paper Perry deals with a sample of Brown Rats (*Rattus norvegicus*) collected in Northern England, mainly in Liverpool, throughout one year. The rats were examined in a thorough and standard way, and simple

statistical treatment of the results is applied. The paper covers such subjects as the sex ratio ; puberty, breeding season and general reproductive physiology of the female (and similar data on the male) ; size of litter, mortality *in utero* and influence of pregnancy on lactation.

As a more detailed example of a point which has been overlooked, let us take this. In 660 females there were 34 per cent. pregnant ; in 158 (*i.e.* 24 per cent.) the embryos were implanted and visible, in 66 they were not yet implanted, and only discovered by washing them out of the uterine horn. Moreover, as embryos may continue to be free for many days if pregnancy occurs during lactation, one cannot state that the ratio of unimplanted to implanted is constant ; one cannot therefore merely observe the number of females in which implantation has occurred, which is easy to observe, and make a calculation for the others. [This is mentioned to show the large and incalculable error that is present in data published by many plague workers.]

ii. The second paper deals with several large samples of house mice from British urban habitats, flour depots, cold stores and corn stacks. Among points of interest are the following : that breeding takes place throughout the year, indeed the proportion of females pregnant is not apparently subject to a seasonal change ; there are significant differences in mice from different habitats in sex ratio, weight at which females attain fecundity, proportion of females pregnant, and annual production of litters. The paper resembles the first, except that it deals with an animal which is more adaptable to differences of environment ; it is an extraordinary fact that the house mouse can live permanently and breed in a cold store at 16°F. (−10°C.). The implications of the work are also carried further, *e.g.* the data on pregnancy and births are used as a base for estimating the number of litters and of embryos per female per annum. *P. A. Buxton.*

Simeons, A. T. W. & Chhatre, K. D. **One Thousand Cases of Bubonic Plague treated in an Emergency Plague Hospital.** *Indian Med. Gaz.* 1946, June–July, v. 81, Nos. 6/7, 235–8.

An analysis of one thousand consecutive cases of bubonic plague should yield percentage results of some statistical significance. This carefully supervised series was taken from a total of 1,039 admitted to hospital, 19 of which were non-bubonic and 20 others had been inadequately treated " before a fixed routine was established ". Sulphadiazine treatment with 61 deaths out of 765 cases was significantly superior to sulphathiazole with 15 deaths out of 131 cases. It is the protective value of a single dose inoculation (2 cc.) of the population with vaccine supplied by the Haffkine Institute which gives rise to doubt. The city population of 110,000 was, as far as one can judge, unselected, for some 90,000 were inoculated, and it appears much more suitable for assessment of the value of this procedure than the rural population, which gave very anomalous results. Moreover the city figures include practically every case of plague that occurred there. It is disappointing then to find that among city cases there is only a difference of 2·62 per cent. mortality rate in favour of inoculated (16·25 per cent.) over uninoculated (18·87 per cent.). Thus the author is compelled to conclude that the value of a single inoculation of 2 cc. of killed vaccine " as a method of reducing the mortality is rather dubious". His further conclusion is that " inoculation as a preventive public health measure cannot even remotely compare with the results that can be achieved with cyanogas, rat-baiting and anti-flea measures ". It is dangerous to depend too much on inoculation. Two points, however, seem to require further investigation ; that of the single dose and that of the killed vaccine. *W. F. Harvey.*

MACCHIAVELLO, A. **Plague Control with DDT and " 1080 ". Results achieved in a Plague Epidemic at Tumbes, Peru, 1945.** *Amer. J. Pub. Health.* 1946, Aug., v. 36, No. 8, 842–54, 1 graph & 1 plan.

Plague is an excellent example of a disease which involves several factors, several links in a chain of events, before it appears in epidemic form. An attack may be made on one or more of these links, upon the rodent reservoir and the insect vector, or better still on both of these. This article is specially directed to the use of the pulicide DDT and the raticide sodium fluoracetate (" 1080 "). It reinforces its argument and its conclusion that " the application of DDT, followed by poisoning with 1080, promises to be the procedure of choice in the control of epidemics of bubonic plague ", by taking as example an epidemic in the city of Tumbes, Peru. The campaign was successful, for the epidemic was stopped 4 days " after finishing the first application of DDT." That was a remarkable result, for a city, the capital of a Department, with 10,000 inhabitants which had no sewers, no public water system ; which was liable to flooding in the rains so that the houses, of bamboo, wood and mud, had to be raised above ground, " leaving spaces beneath which are rat harborages ". The rats were *R. rattus alexandrinus* (95 per cent.) and *R. rattus rattus* (5 per cent.) and the fleas were *X. cheopis* (97 per cent.). Table 2 is a diary of the occurrence of plague cases, 40 all told, from October 7 to January 26, although it is probable there were some unrecorded cases of plague toward the end of September. Application of 10 per cent. DDT powder to the floors of public and private dwellings took place from November 30 to December 10 and " the inhabitants were told not to sweep out the houses for at least a week ". Then came the period of what is called " subsurface application ", with 5 per cent. DDT fron the 11th to the 19th December " between ceilings and roofs, double boundary walls, beneath floors, in corridors and passage-ways used by rats ". The DDT mixed with flour even in strength of 2 per cent. exerted its lethal effect, a strictly contact effect, and on flies and other diptera except mosquitoes. Mention is made of the " toxicity of 10 per cent. DDT for rats (which regularly and carefully lick their fur) in dosages of 1·0 to 2·0 gm. of the powder applied to the body surfaces of the rat " and, as a secondary poison, of the toxicity of 1080 for rat fleas sucking the blood of poisoned rats. This subject will be dealt with later. In the application of 1080 as raticide the city was divided into 9 sectors and the poisoned baits—cakes, rolled oats or water—were placed in all likely situations. The baits of rolled oats were made up in doses of 3 or 4 gm. " poisoned with 1080 in the proportion of 5 parts of poison per 1,000 ". Care had to be taken to keep the baits " out of reach of children and domestic animals ". No accidents occurred to human beings, but a few cats were killed. Many other details are given of the use of this double and direct measure in which both pulicide and raticide have been almost the only agents in a successful plague campaign. *W. F. Harvey.*

GOUCK, H. K. **DDT to control Rat Fleas.** *J. Econom. Entom.* 1946, June, v. 39, No. 3, 410–11.

A dust consisting of 10 per cent. DDT in pyrophyllite was successfully used against fleas on rats in stores and in an infested poultry run. The fleas killed included *Xenopsylla cheopis*, *Leptopsylla segnis*, *Nosopsyllus fasciatus*, and *Echidnophaga gallinacea*. About 1 to 2 oz. of dust were blown down each rat hole.

The following ingenious control method was also employed : Cylinders of roofing paper, 12 in. long and 3 in. in diameter, were prepared. The DDT was applied to strips of cheese cloth, which were then folded and suspended from the

roof of each cylinder. The cylinders were then thrust into rat holes so that rats running in and out dusted themselves with DDT. In practice, however, this method was found no better than simple dusting. *J. R. Busvine.*

CHOLERA.

WOODWARD, L. K. **Condition simulating Appendicitis following Cholera Vaccine Inoculation.** *U.S. Nav. Med. Bull.* 1946, Sept., v. 46, No. 9, 1377–8.

This paper presents an interesting and somewhat disturbing object-lesson, in differential diagnosis between a medical condition and one requiring surgical intervention.

Cholera vaccine (8,000 million per cc.) was administered subcutaneously to 1,100 men in a U.S.N. ship, in two doses of 0·5 cc. and 1·0 cc., with eight days interval.

From 2 to 5 days later, 38 men developed clinical manifestations very closely resembling appendicitis, localized pain and tenderness being prominent. These features persisted for 3 to 16 days, with an average of 7. In the vast majority of cases, the leucocyte count was about 10,000 or more per cmm., though no unusual change in the differential count was noted. Other examinations revealed no significant information.

The condition developed after the first inoculation in 20 cases, and after the second in 18. The clinical features were not exaggerated by a second inoculation in those who showed them after the first (although the second dose was withheld from about one-third of the men).

In 3 cases the appendix was removed. Two patients showed only slight inflammation of the appendix, whilst the third had marked infection and oedema. All three had a striking mesenteric lymphadenitis. Histopathological facilities were not available.

The fact that two of the men had had previous appendicectomy suggested some other aetiological factor. Since then, the author's experience has been confirmed by similar results seen by his colleagues elsewhere. In one instance, nearly all the men receiving cholera inoculations developed a moderate to severe diarrhoea, of some days' duration, a few days later.

The author concludes, with considerable evidence to support him, that the conditions described resulted from the cholera inoculation.

[This is an important observation in the interests of medical officers who are encountering the practice of anti-cholera inoculation for the first time, since the deceptive clinical features might readily lead to a diagnostic error, having serious implications.] *H. J. O'D. Burke-Gaffney.*

BACILLARY DYSENTERY.

THOMPSON, C. M. & WHITE, B. V., Jr. **Shigellosis Studies. III. Clinical Observations on Dysentery caused by** *Shigella flexneri III.* *U.S. Nav. Med. Bull.* 1946, June, v. 46, No. 6, 901–10.

A considerable epidemic of bacillary dysentery occurred in September 1945 among naval units in Tokyo Bay, some 1,300 persons being affected at the height of the outbreak, without, however, any reported deaths; men in shore installations appeared to be free from the disease.

From 20 out of 60 patients studied in detail, *Shigella flexneri III* was isolated. In 78 per cent. of the cases the onset of the illness was acute, with chill, fever of 101°–105°F., and abdominal cramps, followed after some hours by watery diarrhoea; while in 18 per cent. there was an atypical coryzal onset, with headache, myalgia, and rhinitis or sore throat. In both types the acute febrile onset was misleading; the abdominal tenderness with muscular spasm in the abdominal wall in some cases simulated appendicitis, while the acute febrile onset with coryzal symptoms suggested the onset of an acute catarrhal fever or of virus pneumonia.

Following the initial chill and fever, all cases developed diarrhoea, which in the earlier stages consisted of frequent watery stools with abdominal cramp, later giving way to less frequent but bloody stools with tenesmus; dehydration, loss of weight, and glossitis followed.

All patients examined sigmoidoscopically showed a brilliant red injection of the mucous membrane, in most cases with marked oedema, characteristically accompanied by spasm and rigidity of the bowel wall. In the early stages there was a scanty mucoid exudate which later became serous, sanguineous or purulent in association with multiple pin-point necrosis of follicular areas, and secondary infection of the bowel wall. Finally, the exudate became mucoid or muco-purulent, and the mucous membrane oedematous, with a cobble-stone appearance representing the stage of indolent repair.

Most of the patients remained on the sick list for about 19 days, but the duration of the disease was very variable. The first sign of improvement was recovery of appetite, followed by a lessened frequency of diarrhoea and tenesmus. Complete convalescence was protracted, most patients appearing to require several months to regain full strength and weight.

Sulphonamide therapy was not employed as a routine, as the strain was known to be sulphonamide-resistant; in the few cases in which sulphadiazine was used it failed to influence the temperature or symptoms. The basis of treatment was, therefore, maintenance of protein and electrolytic balance, with rest for the affected bowel, by means of a liquid diet supplemented by intravenous saline, dextrose, plasma and whole blood. Diarrhoea, cramps and tenesmus were treated with bismuth, opium and warmth. After the acute diarrhoea had subsided, rectal lavage with warm physiological saline solution seemed to hasten recovery and reduce proctospasm.

In view of the influenza-like onset of many of the cases, and the occasional appearance of herpes, the authors wonder whether a virus may have been associated with the *Shigella* organism as a contributing or predisposing aetiological agent. Epidemiological studies suggested that the disease was spread chiefly by food handlers. *F. Murgatroyd.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

HARGREAVES, W. H. **Amoebiasis.** *Practitioner.* 1946, Aug., v. 157, No. 938, 93–100, 2 figs. on pls. [17 refs.]

This general account of amoebiasis is written for practitioners of medicine in Britain in view of the wholesale infection of troops and others overseas during the late war. It is orthodox and adequately comprehensive, but contains nothing original. *A. R. D. Adams.*

HAYWARD, G. W. **Amoebiasis in Italy.** *Brit. Med. J.* 1946, Sept. 28, 457–9.

The clinical picture of amoebiasis in Italy is different from that seen in India and Burma. The more obvious dysenteric symptoms are usually absent, and the cases, once diagnosed, are amenable to treatment, the relapse rate being low. Amoebiasis (252 cases) accounted for over half the admissions of those suffering from the diarrhoea-dysentery group of ailments in a Medical Division, and was two and a half times as common as malaria. Diarrhoea had been suffered by 204 (81 per cent.) of the 252 patients, and in 70 was evident on the patients' admission ; 106 (42 per cent.) gave a history of abdominal discomfort or upset ; and it was usual, on close questioning, to obtain a history of other more vague manifestations of ill-health. Thickening or tenderness of the caecum was present in 63 per cent. ; 70 per cent. showed abnormal findings on sigmoidoscopy ; and all the cases were specifically diagnosed by identification of vegetative *E. histolytica* in the stools. The recovery of these organisms was difficult until a system of vigorous purgation (calomel grains 5 at night followed by magnesium sulphate at 7 and 9 o'clock the following morning) followed by repeated stool examinations was adopted. " An unusual finding in this series was the infrequency with which amoebic cysts were found in the stools—5 per cent. of the cases only."

With the standard M.E.F. course (injections of emetine grain 1 and Quinoxyl 2½ per cent. enemata daily for 10 days ; Carbarsone 0·25 gm. twice daily for 8 days ; and then E.B.I. grains 3 for 12 days) or the C.M.F. course (emetine grain 1 daily for 3 days ; E.B.I., grains 3 concurrently with Quinoxyl 2½ per cent. enemata for 10–12 days ; and then Carbarsone 0·25 gm. twice daily for 8 days) " the depressing results from standard courses of treatment reported from India and Burma have not been experienced in Italy." Only two cases were determined to have positive stools three weeks after treatment ; but although a proper follow-up of all cases was not possible, nine were known later to relapse.

After some observations on the need for thorough treatment to eradicate an *E. histolytica* gut infection the author refers to the difficulties in the diagnosis of amoebic hepatitis, of which he saw six examples in his series of cases. The picture was here complicated by the fact that an attack of infective hepatitis may leave a permanently enlarged liver. He concludes with the observation that vague abdominal symptoms in a returned soldier should lead to a suspicion of amoebiasis, which can be quickly detected by sigmoidoscopy and examination of the stools after brisk purgation. " There is some doubt whether it is justifiable to institute a long and unpleasant course of treatment in amoebic ' carriers ', where the only positive finding is the presence of cysts of *E. histolytica* in the stools," but it has been the author's practice to treat such infections.

[On the evidence presented there seems to the reviewer no real reason to believe that the amoebiasis described by the author in Italy substantially differs in its course and response to treatment from that found elsewhere. The fundamental difference between these particular cases and those very severe cases encountered in India and Burma, some but not all of which have proved difficult to treat, would appear to lie in the conditions under which the infection was acquired and treated. One series, the Italian, occurred under reasonably good conditions of life ; the other occurred under the conditions obtaining in jungle warfare—with all that entails in lowered resistance, concurrent infections, and lack of early hospitalization facilities. The apparent paucity of cyst-formation in these Italian cases needs substantiation before acceptance, as it is at variance with the usual findings in Italy and elsewhere.]

A. R. D. Adams.

TALLANT, E. J. & MAISEL, A. L., with technical assistance of M. Ruth RAKESTRAW. **Amebiasis among the American Armed Forces in the Middle East.** *Arch. Intern. Med.* 1946, June, v. 77, No. 6, 597–613. [Refs. in footnotes.]

The authors give an account of their experience with amoebiasis in an American army hospital in the Middle East during the two-year period November 1942 to November 1944. Among patients admitted, 464 were diagnosed as amoebiasis, but only a small percentage of these were suffering from dysentery. About 58 per cent. had loose stools or diarrhoea, and about 41 per cent. normal stools, at the time of admission. Of the acute amoebic cases only 18·1 per cent. had dysenteric stools. It was found that 22 per cent. of the Native workmen had *E. histolytica* infection. Of the hospital personnel, consisting of 77 American soldiers, monthly examinations carried out during the two-year period showed that infections first became evident during the second year, by the end of which they were detected in 36·4 per cent. Of cases examined sigmoidoscopically, 10·1 per cent. of patients with acute amoebiasis, 10·2 per cent. of those with chronic amoebiasis and 75 per cent. of carriers had an apparently normal intestinal wall. Of the appendicectomies carried out during the period, amoebic involvement of the appendix was detected in 3·2 per cent. Treatment was carried out with various combinations of intramuscular emetine, carbarsone, diodoquin and chiniofon. In most cases a cure was obtained, but some proved resistant. In some it was difficult to decide whether relapse or reinfection had occurred. *C. M. Wenyon.*

CHAUDHURI, R. N. & CHAUDURI, M. N. R. **An Analytical Study of Intestinal Protozoal Infection with special reference to Amoebiasis.** *Indian Med. Gaz.* 1946, June–July, v. 81, Nos. 6/7, 230–34.

In the decade 1925–1934, 9,015 patients suffering from various complaints were admitted to the hospital attached to the Calcutta School of Tropical Medicine. The patients were mostly Indians, but there were some Europeans and Anglo-Indians. The stools of all were examined, and 2,361 (26·2 per cent). of the patients were found to harbour intestinal protozoa ; 796 (8·8 per cent. of the total) of these were infected with *E. histolytica.* A table is given showing the incidence of the other intestinal protozoa, none of which was as common as *E. histolytica.* Double, triple and even quadruple protozoal infections were encountered, and the numbers of patients discharging vegetative and cystic forms respectively of the various parasites are detailed. Intestinal helminthic infections were found in 226 (nearly 10 per cent.) of the 2,361 patients infected with protozoa ; hookworm infestation, by far the most prevalent of these, was discovered in 159 of them. Some data are given showing the more important intestinal bacterial infections encountered. Charcot-Leyden crystals were found in 119 cases of *E. histolytica,* and in 55 of other protozoal infestations. Amoebiasis was most prevalent in the third and fourth decades of life, and at the extremes of age occurred in two patients aged two years, and in nine aged over sixty years. Of the 796 patients with amoebiasis, 51 per cent. attended hospital for abdominal troubles and the remaining 49 per cent. for other diseases. Of those patients with amoebiasis who had abdominal troubles, 63·8 per cent. had classical dysentery (blood, mucus, or both in the stools) and the remainder suffered from diarrhoea, constipation, abdominal pain, hepatitis or alternating diarrhoea and constipation.

Various treatments were employed for the amoebiasis, and the drugs used included emetine parenterally ; E.B.I., Kurchi liquid extract, K.B.I., tabloid Kurchi, and Stovarsol orally ; Yatren by mouth and as a retention enema ;

4876 (an arsenical) and Carbarsone orally. The " results indicated that most of the drugs used singly are on the whole weak amoebicides. The best results were obtained with Carbarsone," the failure rate being only 9 per cent. with this drug when used alone. *A. R. D. Adams.*

Hopkins, D. L. & Warner, Kay L. **Functional Cytology of** *Entamoeba histolytica*. *J. Parasitology*. 1946, Apr., v. 32, No. 2, 175–89, 4 figs. [29 refs.]

In this paper the authors describe the results of their study of the cytology of *Entamoeba histolytica* in its relationship to locomotion and pseudopodium formation, ingestion and digestion of food and the excretion and egestion of waste products. It is shown that *E. histolytica* thrives best at a redox potential below that which is required to reduce neutral red to colourless form (about −0·4V). Greater reduction than this is associated with encystment, while greater oxidation is injurious and is associated with degeneration. Food is ingested at a point just anterior to the posterior end, while digestion is due to the action of enzymes which are carried to the food vacuoles in digestive spherules which arise at the periphery of the nucleus. The movements of the amoeba are the result of a cycle of changes as in *Amoeba proteus*, in which there is a change from gel to sol posteriorly and from sol to gel anteriorly. The liquid plasmagel is forced forwards by contraction of the outer layers of gel. It passes or bursts through the anterior gel and forms a hyaline cap beneath the plasmalemma. In this way, pseudopodia are formed. It is of interest that the authors find that the various changes which take place at 37°C. do so equally well at ordinary laboratory temperature of about 24°C., but occur more slowly, there being no indication that the behaviour was abnormal at the lower temperatures.

Other subjects discussed include the chromatoid bodies, osmotic activity of cytoplasmic inclusions and the failure of vital dyes to help in the study. The paper, which is illustrated by a series of text figures, must be studied in detail by those interested in the physiology of *E. histolytica*. *C. M. Wenyon.*

Shih Lu Chang. **Studies on** *Entamoeba histolytica*. **IV. The Relation of Oxidation-Reduction Potentials to the Growth, Encystation and Excystation of** *Entamoeba histolytica* **in Culture.** *Parasitology*. 1946, Jan., v. 37, Nos. 1/2, 101–12, 1 fig. & 9 graphs.

In previous papers [this *Bulletin*, 1943, v. 40, 310, and 1944, v. 41, 217] the author has given an account of his studies on the effect of hydrogen-ion concentration on the process of encystation of *E. histolytica* in culture and the importance of the bacterial flora in maintaining a *p*H range favourable for encystation and multiplication of the amoebae. In the present paper are described the results of observations on the oxidation-reduction potential in cultures, and the influence this has on the biological activities of the amoebae. The somewhat complicated technique for carrying out the observations, and the apparatus employed, are fully described with the aid of a diagram, while the results are illustrated in a series of graphs.

It was found that the best growth of trophozoites occurred at potentials between −350 and −425 mV, and that with a rising potential there was a decreasing multiplication till it ceased between −50 and −150 mV. Trophozoites died after an exposure of 12 hours to potentials between −50 and +50 mV ; they died and disintegrated in two hours between potentials +100 and +200 mV. It was also noted that the longer the potential remained below −150 mV the longer did the culture remain positive, and it was only at this potential or lower that excystation would occur. Mass encystation occurred

if, after a period of active multiplication of the amoebae during 22–24 hours, there followed a sharp rise of potential. If immediately after the sharp rise there was a fall in potential, the cysts failed to become mature and disappeared in about 12 hours. Following rapid multiplication of amoebae at very low potentials, smaller amoebae and cysts were produced than when less rapid multiplication and encystment occurred at higher potentials. In certain cases in which mass encystment failed to occur, or when it did occur the cysts failed to become mature, artificial creation of sharp rises of potential by oxygenation enabled these processes to take place. The *p*H values in cultures at the time of encystation varied from 6·4 to 6·8. Mass encystation failed to occur if the *p*H was 7·2 or higher. It appears that, in spite of an intrinsic tendency for amoebae to encyst, they will not do so unless the *p*H is suitable and unless there is a change of potential from one more favourable to one less favourable. These conditions are supplied by the bacterial flora, but it is hoped that a means may be found of providing them without the help of bacteria. *C. M. Wenyon.*

VON BRAND, T., REES, C. W., REARDON, Lucy V. & SIMPSON, W. F. **Chemical Studies on Egg-White Medium for the Cultivation of** *Endamoeba histolytica*. *J. Parasitology*. 1946, Apr., v. 32, No. 2, 190–96, 2 figs.

When *E. histolytica* is grown in a diphasic medium, that is, one consisting of a solid base with a liquid overlay, the amoebae depend for their nourishment very largely upon the substances which diffuse from the solid to the liquid parts of the medium. The authors have investigated the diffusion of various substances in relation to the quantity of overlay and the length and temperature of storage of the medium. In the experiments the standard medium has consisted of three parts of egg white in one part of Locke's solution inspissated to form the base, and Locke's solution for the overlay. It was found that relatively large amounts of reducing substances, essentially glucose, and of nitrogenous materials, essentially ovomucoid, diffuse from the egg-white base into the overlay, but that very little ether-soluble material does so. It was found that the diffusion of the reducing substances was more rapid than that of the nitrogenous material. The quantities of these substances in the overlay varied with the length of storage and with the temperature. It was evident that for comparative studies it would be advisable to use medium which had been stored for the same length of time and at the same temperature. It is felt that the data given in the paper may be of use in the standardization of media for the culture of *E. histolytica*. *C. M. Wenyon.*

HITCHCOCK, Dorothy J. & RAWSON, G. W. **The Use of Dehydrated, Coagulated Egg Yolk in the Preparation of a Medium for culturing** *Endamoeba histolytica*. *J. Parasitology*. 1946, Apr., v. 32, No. 2, 170–74, 1 fig.

The authors describe the preparation of liquid media from dehydrated coagulated egg-yolk for the cultivation of *E. histolytica*. The quantity of egg-yolk used varied from 0·4 per cent. to 3·2 per cent. The final medium was entirely liquid except for the added rice starch. Two strains of *E. histolytica* were tested. One of these, which was growing with a single bacterial organism (organism " t "), failed to grow in any of the tubes inoculated. The other, which was growing with a mixed bacterial flora, grew in tubes containing medium prepared with 1·6 per cent. egg-yolk, but not less. The growth was correspondingly greater with increasing quantities of egg-yolk. Sixteen sub-cultures were successfully made. *C. M. Wenyon.*

SIRTORI, C. & ZORZOLI, G. Le false amebe dell'intestino e della vescica. [**"False" Amoebae in the Intestine and Bladder.**] *Boll. Istituto Sieroterap. Milanese.* 1945, Jan.–June, v. 24, 85–106, 11 figs. on 7 pls. [18 refs.]

In this illustrated article the authors draw attention to the frequent presence in faeces and urine of false amoebae which may give rise to erroneous diagnosis of *E. histolytica*. In faeces these appear in cases of colitis and after repeated purging with salines or phenolphthalein, while in urine they occur in cases of cystitis and after administration of urotropin. The false amoebae are not derived, as usually claimed, from macrophages but from epithelial cells which have undergone various types of degeneration. The swollen nuclei of these cells with their vacuoles and nucleoli stained by bile pigments may appear like amoebae with ingested red blood corpuscles. In no case should a diagnosis of *E. histolytica* be made unless the characteristic nucleus can be seen quite distinctly. *C. M. Wenyon.*

ANDREW, R. **The Clinical and Pathological Features of the Dysenteries.** *Med. J. Australia.* 1946, Aug. 31, v. 2, No. 9, 289–311, 5 figs. [27 refs.]

This Stowell Prize Essay for 1945 contains a good general account of the classical bacillary, protozoal and helminthic dysenteries, with a description of some illustrative cases seen by the author among Australian troops in the Middle East, New Guinea and Australia. It contains no original contribution to the subject. *A. R. D. Adams.*

CANAAN, T. **Hepatic Complications of Amoebiasis.** *J. Palestine Arab Med Ass.* 1946, Sept., v. 1, No. 6, 161–71. [29 refs.]

Intestinal amoebiasis has long been known to be common in the coastal plains of Palestine. The author found 27·5 per cent. of 550 persons to harbour *E. histolytica*. Less than one-third of the 152 infected persons had active intestinal symptoms attributable to the infection at the time of examination. Of 520 other unselected patients examined for liver enlargement or tenderness, 78 per cent. gave a history of dysentery or of diarrhoea; 46 of the 520 had liver enlargement, and in 18 of these the liver enlargement was thought by the author possibly to be attributable to amoebiasis, although in only two of these 18 cases did the liver diminish in size after emetine injections; one of these two had a concurrent cholecystitis, which was relieved by the emetine therapy. Analysis of yet another 300 unselected cases submitted to X-ray examination showed that 66 had some liver enlargement; the author discusses the causes of this enlargement, and considers that in no case was it attributable to hepatic amoebiasis. He found, from hospital records in Jerusalem and Bethlehem, that the incidence of amoebic hepatitis and amoebic liver abscess in Palestinian Arabs, during a twelve-year period, was very low (0·265 per cent. of all inpatients, and 0·96 per cent. of those found to harbour *E. histolytica*) in spite of their high rate of intestinal infestation. *A. R. D. Adams.*

ROSE, J. R. **Vaginitis due to** *Entamoeba histolytica.* [Correspondence.] *Lancet.* 1946, Apr. 6, 520.

The two cases described from Fatshan, S. China, are of purulent vaginitis with ulceration of the vaginal wall. In both cases, active amoebae with

included red blood corpuscles were present in all specimens of the pus examined. In one of the cases, in a woman aged 60, there was a mild amoebic dysentery but cysts alone could be found in the stools. In the other case, in a woman aged 41, the bowel condition was normal. The first case was cured by emetine treatment combined with vaginal douches of copper sulphate solution (1: 5,000). The second was similarly treated, but with douches of 1 per cent. chiniofon. The condition was clearing rapidly when the patient left hospital. In neither case was there any evidence of sinus or fistula. *C. M. Wenyon.*

SINHA, H. S. **A Copper Sulphate Flotation Method for the Examination of *E. histolytica* Cysts.** *Indian Med. Gaz.* 1945, Dec., v. 80, No. 12, 619–21.

The method described involves the use of a copper sulphate solution of specific gravity 1035. A small portion of the stool to be examined is emulsified in 1 cc. of physiological saline solution in a cup of 3 cc. capacity. The cup is then filled up with the copper sulphate solution and immediately covered with a slide, which will be in contact with the liquid. In 10 minutes' time one end of the slide is slightly raised and the cup pushed away, the slide being turned over at the same time. The surface of the slide can then be examined with or without a cover glass. In tests carried out, fourfold concentrations of the cysts were obtained. The method of preparation of the copper sulphate solution is somewhat involved, but when this has been prepared the technique appears to be very simple. *C. M. Wenyon.*

MARSDEN, A. T. H. **The Detection of the Cysts of *Entamoeba histolytica* in the Faeces by Microscopic Examination.** *Med. J. Australia.* 1946, June 29, v. 1, No. 26, 915–16.

Symptomless passers of *E. histolytica* cysts are difficult to detect, as their stools have no pathognomonic appearance. The finding of cysts constitutes proof of infection ; failure to find cysts does not constitute conclusive evidence of non-infection, and the matter of infection remains in doubt. Cysts are voided intermittently, and in light infections many stools contain no cysts at all. On the analysis of data provided by examination of stools from their cases the author and his statistical collaborator, Fairfield Smith, find that one cyst will almost certainly be seen in two examinations of stools from a patient passing 1 million cysts a day ; there is an even chance of detecting a cyst from a patient passing 100,000 cysts a day ; but to have an even chance of seeing even one cyst from a patient passing 1,000 cysts a day, 220 stools must be examined. There is, therefore, no practicable way of detecting all chronic infections by stool examination, or of detecting more than a minority of those individual patients voiding 10,000 or less cysts a day. The significance of negative findings on examination of a predetermined number of stools under varying conditions of time, of place, and of degrees of intensity of infection must, therefore, be appreciated. While the detection of every affected individual is thus impossible, an assessment of the proportion affected in a given population can be arrived at by allowing for the fact that with only an " even chance " of detecting cases with a certain intensity of infection, half these will be missed on stool examination.

At Nakompaton P.O.W. hospital, Thailand, six consecutive stools were examined from each of 1,015 patients clinically cured of amoebic dysentery. About one-third of these men were found still to pass cysts. In the author's

view this represented about half the number not sterilized of their infections. From a statistical analysis of their data the author and Fairfield Smith (in an appendix) consider that the optimum number of stools for examination is four, at intervals of one week ; if this is impracticable and consecutive examinations have to be made, six such should be done. Examination of more than one preparation from the same stool increases the chance of detection of cysts so little as not to be worth while. Any patient passing 1,000,000 or more cysts a day should be detected, and there is a 3 : 1 chance of finding those passing 100,000 cysts a day ; lesser degrees of infection become increasingly difficult to detect.

A. R. D. Adams.

HILL, K. R. **Diagnosis of Intestinal Amoebiasis.** [Correspondence.] *Brit. Med. J.* 1946, Oct. 19, 589.

The author refers to the use of " provocative emetine ", which was frequently used in the Services, as an aid to the diagnosis of latent intestinal amoebiasis, and comments on the lack of recent references to it. The method consists of giving 1 grain of emetine hydrochloride intramuscularly or 3 grains of emetine bismuth iodide orally, on the eve of a stool examination, followed in the morning by a purge.

In this way, it is claimed that a patient having previously produced a series of negative stools may well produce an immediately positive result, owing to the stimulatory effect of the emetine on the parasite.

H. J. O'D. Burke-Gaffney.

RAIL, G. A. **The Use of the Sigmoidoscope in the Diagnosis and Prognosis of Amoebic Dysentery.** *J. Trop. Med. & Hyg.* 1946, Aug.–Sept., v. 49, No. 4, 68–9.

This paper epitomizes an experience gained in some 3,000 examinations performed in a year in the dysentery wards of a military hospital in India. In 3 per cent. (out of 300) the correct diagnosis was arrived at by sigmoidoscopy and by removing material for microscopic examination, for in six out of the nine a tentative diagnosis of bacillary dysentery had been suggested. The combination of sigmoidoscopy and microscopy is more efficient than either procedure by itself, though in the majority of cases, the presence of pathological lesions can be demonstrated by the proctoscope. Ulceration and submucosal haemorrhages, either alone or combined, were noted in 211 out of the 300 cases studied. In 17 these lesions were noted beyond proctoscopic range (from 5–11 inches). The first indication of *E. histolytica* infection recorded consisted of small circumscribed deep red areas in an otherwise normal mucosa, and no ulceration appears to have occurred at this stage. When symptoms had been present for some days the most common manifestation consisted of a number of small ulcers scattered throughout the mucosa and surrounded by a zone of erythema. These ulcers were shallow, without submucosal induration.

Atypical appearances were common. The most common complicating factor was diffuse inflammation of the mucosa, at times so severe as to resemble bacillary dysentery. Sometimes it was necessary to obtain scrapings from several lesions before *E. histolytica* could be demonstrated. In one case, a line of submucosal haemorrhages ran obliquely across the bowel with small areas of ulceration.

The author emphasizes the danger of over-confidence in ability to diagnose amoebic dysentery from the appearance of the lesions without recourse to the microscope.

Prognosis depends upon the extent to which the infection has progressed and upon the treatment to which the patient has been subjected. Upon these grounds the following table has been constructed.

Lesions observed after treatment	No. of cases	No. of relapses	Per-centages
Inflammation	76	6	7·9
Ulceration and/or submucosal haemorrhage ...	24	13	54·17
Stricture	2	2	100
Normal mucosa	198	28	14·14

A study of this table reveals no absolute correlation between the sigmoidoscopic appearances and the relapse rate. It would appear that within a period of 21 days relapse is almost as likely to occur in those showing normal, post-treatment, sigmoidoscopic appearances as in those with definite pathological changes. In amoebic stricture the infection cannot be eliminated by a single course of treatment. In the ulceration-haemorrhage group of 24 cases there were 13 relapses, although the control period of three weeks is far too short to assess prognosis. A period of six months is more advisable.

P. Manson-Bahr.

Cropper, C. F. J. **Sigmoidoscopy in Amoebic Dysentery.** [Correspondence.] *Lancet.* 1946, Sept. 28, 473.

This letter is a postscript to a previous article by the author [this *Bulletin*, 1946, v. 43, 38] who revises two points as the result of recent experience.

He now finds that the most satisfactory method for producing a "clear" lower bowel is by a simple weak bicarbonate enema. At the end of 4–6 hours later, whether meals have been taken in the interval or not, all traces of the enema fluid have been almost invariably evacuated or absorbed.

The important point is often overlooked that the evacuant enema must be just of that volume which will produce an effective call to stool: this varies with individual patients, from a pint to considerably more or less.

The application of retention enemata—especially with undesirable methods—within a few minutes of the evacuant enema, not only renders the medicament used almost ineffectual in strength, but is often very trying to the patient.

The author's second point regards diagnosis. In many cases, ulcers are so minute as to appear as tiny points of extreme congestion with an ordinary magnifying lens. Such small groups, either single or scattered, are best examined with a special magnifying attachment (shown to the author by Lt.-Col. A. M. Khan, R.A.M.C.) with which actual tissue loss may be detected.

H. J. O'D. Burke-Gaffney.

Jacoby, H. **A New Amoebicide for Chronic Amoebic Dysentery.** *Indian Physician.* 1946, Aug., v. 5, No. 8, 187–9.

Amesanil Maltex is a quinoxyl compound, 8-hydroxyquinoline-5-sulphonate of soda, containing approximately 28 per cent. iodine. It is non-toxic and does

not irritate the tissues. The standard dose was 45 tablets [strength not stated] within seven days. No other treatment was given to 30 patients with chronic amoebic infection. The results of the trials were fully successful in those who had had previous treatment, as well as in those who had not. All stools, with one exception, became negative after one course of treatment ; the cases were followed up for two to three months.

Amesanil Maltex therefore appears to be the best of the oxyquinoline group of drugs, especially in chronic cases. Encouraged by these results the author also tried the drug in three cases of acute bacillary dysentery, in which, also, it was successful. *P. Manson-Bahr.*

Bull. U.S. Army Med. Dept. 1946, Sept., v. 6, No. 3, 259–62. **Survey of Intestinal Parasites in Soldiers being separated from Service.** [Tropical Disease Control and Laboratories Branches, Office of the Surgeon General, Washington.]

A survey was made at the 4th Service Command Medical Laboratory, Fort McPherson, Ga., on the stools of 4,000 servicemen returned from the tropics. These consisted of 2,760 white and 1,240 Negro soldiers. Allowance is made for the fact that most of these men resided in the south-eastern States before their army service, but it is considered that they serve roughly as adequate controls, compared with those who had not served overseas.

The figures given represent the results of a single stool examination from each man. Orthodox methods of preparing, staining and examining the specimens were employed. Stoll counts were carried out when hookworm eggs were found. Hookworm egg counts varied from less than 100 per gm. to 17,800. In the majority of cases (262), the egg counts were between 100 and 5,000 per gm.

The most prominent findings among the 4,000 examinations were :—

E. histolytica	14·3 per cent.
E. coli	17·9 ,,
E. nana	26·4 ,,
I. bütschlii	3·1 ,,
G. intestinalis	4·8 ,,
Hookworms	11·6 ,,

The other common parasites were each under 1 per cent.

The following three tables are of comparative interest.

Incidence of parasitic infection in soldiers with service only in the United States and those with service overseas.

	Number of men examined	Infected with 1 or more parasites	Infected with *E. histolytica*	Infected with hookworm
		Per cent.	Per cent.	Per cent.
Service in continental U.S. only	1,273	58·6	10·1	7·5
Service overseas ...	2,727	51·6	16·3	13·5
Total	4,000	53·9	14·3	11·6

Incidence of parasitic infection in soldiers grouped according to geographic area of service.

Theatre	Number of men examined	Infected with one or more parasites	Infected with *E. histolytica*	Infected with hookworm
		Per cent.	Per cent.	Per cent.
U.S.A.*	1,317	57·5	10·2	7·3
E.T.O.+	1,347	56·2	18·5	14·8
Pacific	952	46·2	13·2	13·0
C.B.I.=	160	57·5	21·9	11·3
W.H.T.°	27	40·7	7·4	7·4
E.T.O.—P.A.C.// ...	197	49·2	13·7	12·7

* Continental United States and the Western Hemisphere nontropics.
+ Europe, Africa, Middle East and Italy.
= China, Burma, and India.
° Western Hemisphere Tropics.
// Service in both European and Pacific theatres.

Comparison of cases of Endamoeba histolytica *and hookworm infection, by race*

	Men examined		Infected with *E. histolytica*	Infected with hookworm
	Number	Per cent.	Per cent.	Per cent.
White	2,760	69·0	15·7	12·9
Negro	1,240	31·0	11·4	8·8

H. J. O'D. Burke-Gaffney.

Planet, N. G., Cuocolo, R. & de Almeida, W. F. Observações sobre protozoários intestinais humanos em uma zona rural do estado de São Paulo. [**Human Intestinal Protozoa in a Rural Area of São Paulo.**] *Arquivos Inst. Biologico.* São Paulo. 1945, v. 16, 315–36, 4 graphs. [31 refs.] English summary.

In the rural district of Ibiti, São Paulo, Brazil, a survey for intestinal protozoal infections was carried out. In all 889 examinations were made, giving a percentage rate of infection of 0·78 for *E. histolytica* and 12·71 for *E. coli.* The examinations carried out represented about 10 per cent. of the whole population of the district. A comparison is made between the present record and those previously made in Brazil, in which a much higher rate of infection for *E. histolytica* was noted. *C. M. Wenyon.*

Monat, H. A. & McKinney, W. L., Jr. **Giardiasis : Question of Pathogenicity.** *U.S. Nav. Med. Bull.* 1946, Aug., v. 46, No. 8, 1204–6. [13 refs.]

The authors note that in recent years the majority of text-books and publications attempt to connect giardiasis with a definite set of symptoms. In their experience the infection is frequently associated with a syndrome of irritable colon, nausea, vomiting, fullness and diarrhoea, alternately with constipation.

Of thirty cases, two had co-existing hookworm, another had filariasis and malaria, ten had duodenal ulcer, four had *E. nana* and *E. coli* and two *E. histolytica*. Seven had proctoscopic evidence of irritable colon and seven had normal proctoscopic findings; two had jaundice. In these cases it was found that the giardia infection was easily eradicated by treatment with atebrin, stovarsol or carbarsone. In no case, however, did the symptoms disappear with removal of the infection unless they were specifically treated. On this account the authors express their belief that the flagellate is not pathogenic, does not produce any pattern of symptoms, and finds a fertile field on previously irritated gastro-intestinal mucosa and gall bladder. They maintain that in order to establish pathogenicity it will be necessary to infect a perfectly healthy individual and thereby to produce the symptoms attributed to the infection. Such an experiment has never been performed. *C. M. Wenyon.*

WENRICH, D. H. **Culture Experiments on Intestinal Flagellates. I. Trichomonad and other Flagellates obtained from Man and certain Rodents.** *J. Parasitology.* 1946, Feb., v. 32, No. 1, 40–53. [27 refs.]

In this paper the author describes a somewhat novel method of cultivating intestinal protozoa. Instead of making the usual subculture from tube to tube he has added, from time to time, further nutrient material and distilled water. In this manner a great deal of labour has been saved, and cultures have remained positive for surprisingly long periods. The basic fluid most employed was modified Ringer's fluid, or a fractional dilution of ordinary Ringer's fluid. Nutriments were gastric mucin and Loeffler's dried blood serum, usually in 0·2 per cent. concentration. Various flagellates from rats, mice, guineapigs and hamsters were cultivated, as also five strains of *Trichomonas hominis*, four from human cases and one from a dog. Trichomonads indistinguishable from *T. hominis* were found in a number of rodents—rats, house mouse, white-footed mouse, field mouse and the musk rat—but it remains to be shown whether these are physiologically similar to *T. hominis*. In addition to the various species of *Trichomonas*, including two of the four species (one a new one) considered to be present in rats, species of *Retortamonas* (*Embadomonas*) and *Monocercomonoides* (*Monocercomonas*) were successfully cultivated. *C. M. Wenyon.*

WATSON, J. M. **On the Coprophilic Habits of a Ciliate**—*Glaucoma piriformis*. *J. Trop. Med. & Hyg.* 1946, June–July, v. 49, No. 3, 44–6, 1 fig. [12 refs.]

SELIMKHANOV, K. A. [**Balantidial Colitis in Azerbaidjan.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1945, v. 14, No. 4, 70–73. [In Russian.]

The author describes three cases of balantidiasis observed in the course of autopsies carried out over a period of five years in Azerbaidjan (Caucasus). In all these cases there was evidence of a peculiar form of ulcerative colitis associated with the presence of *Balantidium coli* in the affected areas. The ulcers in question were oval in shape, with undermined margins of red colour, due to haemorrhages, while the base was dirty green. The ciliates occurred in the submucosa and in the muscle and serous layers, where they were found in the lumen of the blood vessels and lymphatics. In the mucosa there were deposits of pigment, which is regarded as a product of metabolism of the ciliate. Since balantidial colitis is rarely diagnosed, the author recommends the microscopical examination of stools for protozoa in all cases of intestinal disorder. *C. A. Hoare.*

See also p. 128, FETTES, D., **Surgery in the Tropics.**

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

BALTAZARD, M. Identification des spirochètes récurrents—individualité de l'espèce *Spirochaeta recurrentis*. [**Differentiation of Relapsing Fever Spirochaetes—Individuality of the Species** *Treponema recurrentis*.] *Arch. Inst. d'Hessarek.* Teheran. 1946, May, No. 4, 57–62.

The author claims that *Treponema recurrentis* can be differentiated from the other spirochaetes of relapsing fever. *T. recurrentis* is distinguished by the following characteristics :—it produces large epidemics ; it is motile in human blood ; it infects lice feeding on human cases ; it is infective for monkeys (*Macacus sylvanus*), feebly but constantly infective for white mice, very feebly and inconstantly for white rats and only exceptionally for guineapigs.

These findings were confirmed for the strains of louse-borne relapsing fever isolated during a large epidemic in Iran. Attempts were made to increase the duration and weight of infection in mice by splenectomy before inoculation and by rapid passage, but all proved relatively unsuccessful.

A definite difference in microscopical appearance between *T. recurrentis* and tick-borne relapsing fever spirochaetes was observed with dark-ground illumination. *T. recurrentis* appears as an undifferentiated luminous spiral, whereas the other spirochaetes show a dark centre surrounded by a bright outline. This is only the effect of refraction and no difference can be brought out with vital stains or by staining in fixed preparations.

The author considers this difference to be of great diagnostic value, and he used it as the criterion for deciding that a widely-used laboratory strain of *T. recurrentis* which had been adapted to mice is in fact one of the tick-borne spirochaetes. *J. C. Broom.*

RAFYI, A. *Spirochaeta microti* n. sp., parasite du campagnol (*Microtus sp.*) en Iran. [*Spirochaeta microti* **n. sp. a Parasite of Wild Mice** (*Microtus* sp.) **in Iran.**] *Arch. Inst. d'Hessarek.* Teheran. 1946, May, No. 4, 49–51.

A new species of spirochaete, for which the name *Spirochaeta* [*Treponema*] *microti* is proposed by the author, has been isolated from wild mice in Iran. This organism, unlike *T. persicum*, will not infect rabbits and guineapigs but is highly virulent for white rats. *J. C. Broom.*

QUIN, C. E. & PERKINS, E. S. **Tick-borne Relapsing Fever in East Africa.** *J. Trop. Med. & Hyg.* 1946, Apr.–May, v. 49, No. 2, 30–32.

An account of the clinical features and results of N.A.B. therapy based on observations made on 400 African troops suffering from tick fever in East Africa. The bulk of the cases occurred in transit camps infested with *Ornithodorus moubata*.

The clinical features were typical and included the usual variety of symptoms. In a series of 104 cases, the percentage incidence of various complications was as follows :—iridocyclitis 15 per cent. ; cerebral, 4 ; jaundice, 8 ; lobar pneumonia, 5 ; severe bronchitis, 4 per cent.

Records were kept of 80 cases treated with N.A.B. In doses up to 0·6 gm. this therapy seemed to have little effect on the course of the disease, for the same average of two relapses occurred in these 80 patients treated with N.A.B. and in 49 controls receiving only symptomatic treatment. *E. Hindle.*

RAYNAUD, R. & PÉGULLO, J. Méningo-encéphalite et typhus récurrent. [**Meningo-encephalitis and Relapsing Fever.**] *Algérie Méd.* 1946, May–June, No. 3, 241–2.

This is a report of a case of an Algerian native showing a meningo-encephalitic syndrome, which lasted for five days and was followed by evidence of an extrapyramidal lesion which still persisted after five and a half months.

On the fifth day, *T. recurrentis* was found in a blood film. Six days later, the temperature rose again and was accompanied by a recrudescence of the meningeal syndrome, with treponemata in the cerebrospinal fluid.

To begin with the Wassermann and colloidal benzoin reactions were strongly positive, but when the meningeal manifestations resolved, the Wassermann reaction became negative and the colloidal benzoin test normal.

The author comments on the transitory positive Wassermann and colloidal benzoin reactions whilst the meningeal syndrome persisted and which were "contemporary with the spirochaetal septicaemia".

He also comments on the occurrence of a localized extrapyramidal affection in relapsing fever and considers that "in the aetiology of extrapyramidal syndromes, the organism of relapsing fever takes its place, in this locality, beside the neurotropic viruses". *H. J. O'D. Burke-Gaffney.*

RAYNAUD, R. & PÉGULLO, J. Syndromes extrapyramidal et méningé, seules manifestations d'un typhus récurrent. [**Extrapyramidal and Meningeal Symptoms as the only Features of Relapsing Fever.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1946, Nos. 22/23, 368–70, 1 chart.

FLOCH, H., TAILLEFER-GRIMALDI, J. & DE LAJUDIE, P. Sur la leptospirose ictéro-hémorragique à Cayenne. [**Icterohaemorrhagic Leptospirosis in Cayenne.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 129.* 1946, June, 9 pp., 4 charts (1 folding).

During the last quarter of 1945 and the first quarter of 1946, the authors diagnosed 4 cases of Weil's disease among the patients of the General Hospital at Cayenne.

The cases were all identified by sero-diagnostic tests; these were positive against *L. icterohaemorrhagiae*, but negative against *L. grippo-typhosa*. The clinical symptoms are described in detail and present the usual variations found in this disease.

The main interest of these cases lies in the possibility of their being confused with yellow fever. The authors are of the opinion that some of the cases of jaundice with "black vomit" that have been notified from time to time as suspected cases of yellow fever, were in reality cases of spirochaetal jaundice.

E. Hindle.

BUCHANAN, G. **Spirochaetal Jaundice (Weil's Disease). Does it occur in South Africa?** *South African Med. J.* 1946, Sept. 14, v. 20, No. 17, 507.

"No evidence of spirochaetal jaundice was demonstrated in over 200 jaundiced patients investigated.

"No rats and other rodents examined were found to harbour the causal spirochaete.

"The leptospirae present in local slimy waters produced no ill-effects in guineapigs."

YAWS.

HILL, K. R., FINDLAY, G. M. & MACPHERSON, A. **Treatment of Yaws with Penicillin.** *Lancet.* 1946, Oct. 12, 522–5. [15 refs.]

This paper is based upon 128 cases of yaws in West African women and children. After 20,000 units of penicillin in saline had been given intramuscularly at intervals of three hours for 12–24 hours, primary and secondary skin lesions healed, but some cases later relapsed.

Penicillin in sterilized beeswax (2 per cent.) in ground-nut (arachis) oil formed a lumpy suspension and intramuscularly caused extreme pain. Doses of 100,000 units every 12 hours gave sustained penicillin blood levels of 0·1–0·15 unit, and urine levels of 60 units per cc. throughout 24 hours.

Penicillin dissolved in 1 cc. physiological saline and shaken with 4 cc. sterile beeswax in ground-nut oil, gave a fine emulsion which caused little pain. Doses of 100,000 units 12-hourly gave blood urine levels similar to those of penicillin in saline alone [0·1 unit at 3½ hours] but sustained 2–3 hours longer. In most cases the penicillin dosage was 100,000 Oxford Units in "oil once or twice daily." There was no difference in results after the use of the sodium or calcium salt. No Herxheimer reactions were observed.

Primary lesions (15) usually became dry in 24 hours. Healing was observed within 48 hours and was complete in 9 days. One case failed to respond immediately and one of 6 cases followed up for three months had relapsed. In 5 cases the Kahn reaction was reversed in two weeks to seven months.

Secondary lesions were seen in 96 patients; 81 completed the course. Clinical cure was observed in 8½ days. Of 63 cases followed up for three months two had relapsed, and of 45 followed for 4–6 months one had relapsed. None of 21 followed for 7–12 months had relapsed. The serological response was as follows: of 40 cases after three months the Kahn reaction was negative in only one; of 31 after 4–6 months in only 4; and of 19 after 9 months in only two cases.

In 6 secondary cases spirochaetes disappeared from 9–24 hours after starting treatment with penicillin in saline. The doses which these patients received ranged from 50,000 to 200,000 units.

Tertiary lesions (17 cases). Of 17 cases with bone lesions 11 showed remission of symptoms and great improvement in osseous signs in 16½ days; two did not respond. Six cases which were followed for periods of 4–12 months had not relapsed. [There is some uncertainty in the statement of a clinical relapse with a negative Kahn reaction. Goundou is probably a secondary, not a tertiary, lesion. There is no mention of secondary cases with bone lesions.]

The number of cases treated with both arsenicals and penicillin is too small for any conclusions regarding the merits of combined therapy.

The immediate effect of penicillin in the doses used was a more rapid healing of skin, and perhaps of bone lesions than with arsenicals, but the ultimate effect on serological reactions is not, perhaps, much superior.

The authors recommend 100,000 units of penicillin in ground-nut oil and beeswax given intramuscularly each day for 10 days, and that trial should be made of penicillin followed by arsenicals.

[See also DWINDELLE, REIN, STERNBERG and SHELDON, this *Bulletin*, 1946, v. 43, 1043.] *C. J. Hackett.*

RADNA, R. Sur le traitement de la stomatite bismuthique par l'acide ascorbique. [**Treatment of Bismuth Stomatitis with Ascorbic Acid.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, Nos. 1/2, 105–6.

Stomatitis following bismuth therapy is fairly common amongst the Natives of the Belgian Congo. Despite all precautions, some 2 to 3 per cent. of all

patients having bismuth treatment (without arsenic) develop stomatitis. The cases are often very resistant to the usual forms of treatment. The author therefore attempted to treat several severe cases with large doses of vitamin C.

He describes two cases of yaws, which had been treated with about 15 cc. of an oily suspension of 10 per cent. " dermatole " [presumably bismuth subgallate] in 8 weeks. Each had a serious stomatitis, one patient being hardly able to eat. Ordinary measures were useless. Each patient was then given 0·5 gm. of ascorbic acid intravenously in daily doses for 10 days, together with local treatment by painting with 5 per cent. methyl violet.

In three days, improvement was marked : at the end of a week, the swelling of the gums had subsided ; by the end of a fortnight, the buccal mucosa had returned to normal.

Encouraged by these results the author has treated seven other cases of severe stomatitis, due to bismuth and to mercury, and has obtained rapid healing in these cases also. *H. J. O'D. Burke-Gaffney.*

LEPROSY.

Oteiza Setien, A., Ibarra Perez, R. & Gonzalez Prendes, M. A. Censo de lepra en Cuba (Estado actual, Junio de 1946). [**Leper Census in Cuba, June 1946.**] *Rev. Sifilografia, Leprologia y Dermatologia.* Marianao, Cuba. 1946, Apr., v. 3, No. 2, 68–109, 10 figs.

The authors begin this article by a brief review of previous records of leprosy in Cuba. In 1926, a census was begun and 140 cases were reported, but " the record was incomplete." In 1932, notes were made of patients attending the dermatological section of Reina Mercedes Hospital, and in 6 months 23 cases of leprosy were seen. Other records studied were the deaths due to this disease between 1902 and 1932 inclusive ; they totalled 1,067. Among the causes for failure on the part of doctors to report cases some are trivial ; one said that if he did so he would make enemies of other members of the family, another that it would lose him votes at a forthcoming election. In other cases patients conceal their disease or go to unqualified persons for fear of being reported and isolated.

To obtain more accurate figures centres were set up over the island by the Ministry of Health through the sub-committee entrusted with the Prophylaxis of Syphilis, Leprosy and Cutaneous Diseases, and during 1945 there were 199 new cases which had not been previously reported. Moreover, it was demonstrated that insufficient importance was attached to the disease in Cuba, and that many persons with leprosy were going about unmolested.

As a result of the census now undertaken, 6 groups were recognized : (1) Ambulatory cases. (2) Hospitalized cases. (3) Lepers provisionally discharged. (4) Those living with lepers. (5) Healthy children of lepers. (6) Those who had died. Tables are given of the figures in different municipalities of ambulatory cases in the various Provinces. Altogether there were 2,166, of whom 1,233 were males and 933 were females ; the rates varying from 1·63 to 6·0 per 10,000. Patients were hospitalized in the National Sanatorium San Luis de Jagua (311) and in the San Lázaro Hospital (325) ; 636 in the whole Republic being in hospital. The number on provisional discharge cannot be stated with accuracy. The intimate contacts (1,346) of 375 lepers were examined and 45 (3·34 per cent.) were found infected. Children born to lepers in hospital are taken away at once and sent to be brought up at the home of some relative of the parents. No records can be traced earlier than 1936 ; in

the ten years there have been six births at the San Luis de Jagua and 19 at San Lázaro, 25 in all, 15 boys and 10 girls; 15 white, eight half-castes and two negroes. In June 1945, 19 were living, two had died at birth and four within a few months of birth. A proper Preventorium to which the children might be sent is greatly needed and would be far preferable to boarding the children with relatives of the patients. The number of lepers registered as dying in the decade 1936–45 was 535. This includes those who died in hospital or in their own homes. Nearly half, 250, were between 31 and 50 years of age, four were under 15, 163 were between 51 and 70, and 40 were over 70; 401 were males, 134 were females. *H. Harold Scott.*

HELMINTHIASIS.

DE OLIVEIRA, P. P. Helmintíase e anemia no meio militar. [**Helminthiasis and Anaemia in a Military Establishment.**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Oct., v. 2, No. 10, 835–9. English summary.

The faeces of 445 men in an artillery regiment were examined by the Stoll method for helminthic infestation, and 441 (99·1 per cent.) were positive. *Ascaris lumbricoides* was present in 425 (94·6 per cent.), *Trichuris trichiura* in 336 (74·8), *Necator americanus* in 323 (71·9), *Strongyloides stercoralis* in 27 (6·01) and schistosomes in 2 (0·44). [All the percentage figures except the last, are wrongly stated in the text.] For treatment three drugs were used: Cristoids containing 0·2 gm. of hexylresorcinol; Panvermin capsules (perolas) containing carbon tetrachloride 4 drops, oil of chenopodium 4 drops, chloroform 1 drop and phenolphthalein; and L.Q.F.E. vermifuge (Laboratorio Químico Farmacêutica do Exercito) which contains "essence" of chenopodium 2 drops, chloroform 1 drop, podophyllin and phenophthalein [amount not stated]. The complete courses of these were 5 cristoids on two successive days, 12 capsules of Panvermin or 10 of L.Q.F.E., with a second course after an interval of 12 days. 251 patients received the cristoids, 123 the Panvermin, and 63 the L.Q.F.E. [these total 437 patients]. It was found that Panvermin was the most effective for *Necator americanus*; the cristoids less effective and the chenopodium alone the least. Those with *Strongyloides* infestation resisted the above forms of treatment, and gentian violet, (merexylan Wander), was substituted, 0·06 gm. tablets, 3 daily for 20 days; subsequent examination of faeces failed to discover any ova.

For the anaemia, 4 preparations were tried, the sulphate and chloride of iron, with copper sulphate and with vitamin B. It was found that ferrous sulphate was the best, especially in the form of the "Army laboratory anti-anaemia tablets" which consist of copper sulphate 0·02 gm., ferrous sulphate 0·20 gm., powdered rhubarb 0·20 gm. and excipient. Next best was Ribotiron which consists of ferrous sulphate and vitamin B. *H. Harold Scott.*

STUNKARD, H. W. **Interrelationships and Taxonomy of the Digenetic Trematodes.** *Biol. Reviews.* 1946, Oct., v. 21, No. 4, 148–58. [Numerous refs.]

PINTO, C. & DE ALMEIDA, A. F. Distribuição geográfica e freqüência do "Schistosoma mansoni" no Brasil. [**Geographical Distribution of *Schistosoma mansoni* in Brazil.**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Dec., v. 2, No. 12, 1000–1008. [28 refs.] English summary.

This article is based on the many recorded findings of medical men all over Brazil who have examined the faeces of the people, or who by viscerotome

specimens have found evidence of schistosomiasis. It is impossible to give the names of all the places where the infestation has been found, for the article itself is little more than a list. Suffice it to say that the infestation is very widespread. In the State of Pernambuco there are as many as 65 foci, in Bahia 37, in Minas Geraes 33, in Alagoas 20, in Paraiba 11 and in Sergipe 10; in several other States foci exist, but in fewer places. So far 198 foci have been found. *H. Harold Scott.*

Macfarlane, Dorothy G. & Macy, R. W. *Cercaria oregonensis*, **n. sp., a Dermatitis-producing Schistosome Cercaria from the Pacific Northwest.** *J. Parasitology.* 1946, June, v. 32, No. 3, 281–5, 1 fig.

The authors investigated in 1943 and 1945 the cause of the severe dermatitis occurring in a man after swimming in the lake in the campus of Reed College, in the Portland area of Oregon. The dermatitis was ascribed to a new species of cercaria which is described. For the details of the structure of this species the paper itself must be consulted. The only local snails that were found infected with it belonged to the species *Physa ampullacea* (Gould).

This addition to the species of cercaria which can cause dermatitis of man may be confused with *Cercaria elvae*, but it is not likely to be confused with the other species known to cause this disease. After leaving the snail *C. oregonensis* swims to the lightest part of the container; it may remain motionless in the light area of the container, but usually it attaches itself to the side of the container by its ventral sucker. *C. oregonensis* emerges from the snail between 6 p.m. and midnight, while *C. elvae* emerges in the late afternoon. The authors found only mature sporocysts and found them only in the late autumn. Like those of other cercariae of this group they were interwoven with the tissues of the snail and could not be dissected out. Probably there are mother and daughter sporocysts similar to those of *C. stagnicolae* described by Cort and Olivier (*J. Parasitology*, 1943, v. 29, 81).

The dermatitis closely resembled the swimmer's itch common in the North Central United States and in Canada. Attempts to produce it experimentally, by putting the foot or arm into a bucket containing very numerous cercariae, failed; but when several drops of water containing numerous cercariae were placed on the forearms of six persons, the dermatitis was produced in two of these subjects. As the water evaporated the cercariae seemed to penetrate the skin. Intense itching or prickling resulted, which lasted 3 hours. The infected spot was at first red and during the next two days papules appeared and there was discomfort when the skin was irritated by the sleeve; but pustules did not develop. The dermatitis lasted a week in one subject and a month in the other. *G. Lapage.*

Khalil, M. B. & Hilmy, I. S. **The Palm-Leave as a Snail Trap; a Preliminary Report.** *J. Roy. Egyptian Med. Ass.* 1946, Jan.–Feb., v. 29, Nos. 1/2, 1–6.

In order effectively to assess the results of anti-bilharzia campaigns, it is necessary to be in a position to determine quantitatively the intensity of snail infestation in water-courses before and after eradication measures have been attempted.

The authors describe a snail-trap by means of which, it is claimed, the presence of snails and the degree of infestation of a given water collection may be determined with ease and fair accuracy.

The trap consists of a piece of fresh, green and intact palm-branch of constant length (one metre is suggested). The trap is submerged horizontally in the water, and anchored to the bank by a length of string attached, at its other end, to the centre of the branch.

The tip of the branch should point down-stream, and the upper surface of the leaves opposite to the canal bed. (It is suggested that the whole trap, including the string, should be well under the surface, to escape the notice of passers-by, who are apt to take possession of the string.)

After four days, the trap is raised carefully and the snails are collected by placing the palm branch vertically, tip downwards, in a white dish of water. Each leaf is scraped gently to release any snails found on it. The hands should be rinsed in a jug of water from time to time. The authors claim that " it is thus possible to a great extent to avoid infection with Schistosome cercariae. So far it has been found that rubber gloves are not necessary at all " [nevertheless, some simple protection from this obvious danger may easily be improvised].

A rubber sheet is spread under the dish to catch snails which may fall out. When all the leaves have been wiped clean, the contents of the sheet, dish and water-jug are poured into a wire net. The contents of the net are washed in the canal and then sorted and counted on the cleaned sheet or dish, and the snails thrown back into the water. [Presumably to maintain snail population for comparison.]

The authors state that the trap has been used for 16 years, and that snails were collected in large canals, where the wire-net method failed. It was used successfully along the course of the Nile, in the Assuan Dam and in the canals before the Kom-Ombo campaign in 1940.

Two tables are presented, to show the varying sizes of trap, periods of immersion in water, and types of snails caught, which increased with the period of immersion. The second table also compares traps used in pairs at either side of a canal.

The authors state : " It is significant to note that the total number of snails on either trap of each experimental station is almost equal for equally large traps though the number of the corresponding group of snails varies greatly ". They consider, however, that " this variation does not affect very much the predominant snail present in the canal, should there be one."

[The value of the tables is lessened by the fact that the unit of measurement of the traps is not indicated in them.] *H. J. O'D. Burke-Gaffney.*

WELLER, T. H. & DAMMIN, G. J. **An Improved Method of Examination of Feces for the Diagnosis of Intestinal Schistosomiasis.** *Amer. J. Clin. Path.* 1945, Nov., v. 15, No. 11, 496–500.

This paper describes studies on a method of improving the efficiency of the acid-ether centrifugation technique as used for the recovery of eggs of *Schistosoma mansoni* [see also this *Bulletin*, 1946, v. 43, 347]. The point at issue was the liberation of eggs which are trapped in the stratum of floating débris between the acid and the ether, and which therefore fail to reach the egg-bearing sediment after centrifugation. It was thought that the addition of a wetting agent would reduce the adhesive properties of the débris and thus release the eggs.

Twenty-four faecal specimens, each containing relatively large numbers of eggs, were examined by the semi-quantitative acid-ether centrifugation technique and by four modifications of this method. In each modification 0·6 cc. of a 10 per cent. solution of one of four different wetting agents was added to the acid-faeces mixture. In two of the modified techniques the recovery efficiency was much increased. With one of these, in which the wetting agent was Triton NE (a 33 per cent. aqueous solution of polyethyleneglycol monoisooctyl phenyl ether) further studies were carried out to determine the degree of increased efficiency, and also the mechanism. It was proved that the increased

efficiency was due, in part at least, to the release of eggs trapped in the débris. The effectiveness of the routine method, and of the Triton NE modification, were compared when used under survey conditions. Duplicate samples from 500 faecal specimens were examined by the two techniques. By the routine method eggs of *S. mansoni* were recovered from 84 of the specimens ; by the Triton NE modification 105 specimens were positive. *J. J. C. Buckley.*

HALAWANI, A., NOR-EL-DIN, G., SHAKER, M. & KHALEK, F. A. **On the Value of the Colloidal Gold Reaction and Cephalin Cholesterol Flocculation Test in the Study of Liver Damage in Cases of Schistosomiasis.** *J. Roy. Egyptian Med. Ass.* 1946, Jan.–Feb., v. 29, Nos. 1/2, 7–12. [11 refs.]

The authors begin their paper by discussing the results and significance of the colloidal gold reaction and the cephalin cholesterol flocculation test, and they review the literature, with special reference to the cephalin cholesterol test and its mechanism.

They then describe their experiments, designed to assess the value of these two tests in detecting liver damage caused by bilharzial infection and antimony treatment. They chose patients with long-standing infections of intestinal schistosomiasis associated with liver changes and splenomegaly. Urinary schistosomiasis was also studied, and, for comparative purposes, cases of infective hepatitis, obstructive jaundice, malaria and amoebic hepatitis were included.

The flocculation test was done on 135 sera, and the colloidal gold test on 87. For the latter test, MCLAGAN's method was used, and for the former, HANGER's.

Some 85 per cent. of cases of intestinal schistosomiasis were positive by both tests. The cephalin test was found the more sensitive of the two. The authors consider the tests of value in jaundice and cirrhosis and hope to publish results of tests performed before and after treatment of schistosomiasis. The principal results are summarized below :—

Condition	Cephalin flocculation test			Colloidal gold test		
	No. of sera	Positive	No. ++ or above	No. of sera	Positive	No. ++ or above
Apparently free from liver damage	8	5	0	10	1	0
Bilharzial cirrhosis ...	13	11	9	20	17	15
Infective hepatitis ...	32	31	26	65	60	55
Malaria and dysentery ...	3	3	3	11	11	11
Obstructive jaundice ...	6	1	1	7	2	1

H. J. O.D. Burke-Gaffney.

RADNA, R. Contribution au traitement de la bilharziose intestinale. [**The Treatment of Chronic Intestinal Schistosomiasis.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, Nos. 1/2, 87–8.

Although intestinal schistosomiasis usually responds successfully to chemotherapy, a few cases are left with a refractory proctitis, ulcerative or papillomatous,

The author has treated six of such cases with intramuscular injections of histidine, having been impressed by the results of this treatment in other forms of chronic ulceration of the stomach and intestines.

The preparation used was Larostidine, Roche. A complete course consisted of 24 to 36 intramuscular injections, one ampoule [quantity not stated] being given daily for 36 days.

In five cases, the results were satisfactory. The sixth showed slight improvement. One typical case is described fully, in which the rectal ulcers and the symptoms arising from them cleared up completely.

H. J. O'D. Burke-Gaffney.

ESPERSEN, T. Om tilsigtet og uønsket Virkning ved 191 Baendelormekure med Extractum filicis i Doser paa indtil 15 gram. [**Results of treating 191 Cases of Tapeworm Infection with** *Extractum filicis.*] *Nordisk. Med.* 1946, Sept. 27, v. 31, No. 39, 2191–5. [12 refs.] English summary.

In the Royal Frederik Hospital and the Rigshospital, Copenhagen, between 1892–1944, 191 patients were treated for tapeworm; all but 12 were *Taenia saginata* infections, 9 being due to *Diphyllobothrium* and 3 to *T. solium.* No evidence of pernicious anaemia was found. The drug used was *Extractum filicis*: in the last 25 years, it was given in doses up to 15 gm., but since 1933 the maximum dose was reduced to 10 gm.

In 72 per cent. of cases, evacuation of the scolex occurred after the first treatment: the frequency of this was some 8 per cent. greater when 12–15 gm. was used than with a dose of 8–10 gm.

"In a few cases" such toxic phenomena as palpitation, tachycardia, feeling of cardiac oppression and accelerated menstrual bleeding occurred. Severe epistaxis appeared in one case: in two cases a transitory jaundice, and in two others a transitory albuminuria followed a dose of 15 gm.

On the whole, it did not appear that toxic effects from 12–15 gm. were essentially more severe than those following the use of 8–10 gm. In two cases where 10 gm. were given, alarming symptoms followed, but these may have been hysterical. Although the usual contra-indications were not always observed, "no threatening signs of intoxication" otherwise appeared.

Vomiting, diarrhoea and abdominal discomfort did not seem to have a convincing relation to the size of the dose; but general lassitude was rather more common after large doses.

Ten of the patients were children: in them, the outcome of the cure was independent of dosage. Untoward effects did appear, however, in cases where the dose exceeded two-thirds of a gramme for each year of age; and it seems desirable not to exceed this dosage in children.

A table illustrates this latter point, and five other tables show the results, favourable and otherwise, of treatment with the different dosages.

H. J. O'D. Burke-Gaffney.

FORSTER, E. B. **Insanity with Epilepsy following Infestation by** *Cysticercus cellulosae.* [Memoranda.] *Brit. Med. J.* 1946, Oct. 12, 543.

DUNGAL, N. **Echinococcosis in Iceland.** *Amer. J. Med. Sci.* 1946, July, v. 212, No. 1, 12–17, 1 fig. [10 refs.]

The author traces the history of human hydatid disease in Iceland since the middle of the 19th century; for details the original paper should be consulted. He also examined the records of hydatid cysts found at autopsy in hospitals in Reykjavik between 1930 and 1944 inclusive. During these 15 years, 1,231 autopsies were done, omitting still-born children and children under 14 years old, but including two subjects from which hydatid cysts had been removed before death. Among these 1,231 subjects 60 (1 in 20·5) had hydatid cysts.

Table 2 given by the author shows that these cysts were present mostly in those belonging to the higher age groups. None was found in persons under the age of 20 years. Among 98 subjects aged over 70 years cysts were found in 20, and in 151 over 60 years old cysts were found in 41 (16 per cent.), a proportion of 1 in 6. Dungal concludes that in 1913 every sixth person harboured hydatid cysts.

The author regards these figures as being representative of the whole country, because, although they are taken from hospitals in Reykjavik, most of the people of that city were brought up in the country and patients in its hospitals come from other parts of Iceland. A graph of the number of subjects of hydatid disease reported in Iceland between 1896 and 1940 and of the deaths due to this disease since 1911 indicates that in 1940 the number was only one-tenth of that in 1912.

Probably at the end of the last century a third or even half of the people of Iceland had the infestation. This is not surprising in view of the fact that they lived closely with dogs, and knew little about the method of infestation. Krabbe (*Récherches helminthologiques en Danemark et en Islande.* Copenhague, 1866) found *Echinococcus granulosus* in 28 per cent. of Icelandic dogs, which is an infestation rate 47 times higher than that found in Denmark; and there were, in Iceland, 15,000 to 20,000 dogs at a time when there were 70,000 people. Finsen reported that in 1858 it was rarely possible to slaughter an old ewe or cow without finding an echinococcus cyst.

There is, however, little doubt that the younger generation now growing up is practically free from the infestation. The author's autopsy records show this. The cysts are found only in the older people. The decrease is due to education of the people and to anthelmintic treatment of the dogs once a year, which has led also to the disappearance of *Coenurus cerebralis* and other kinds of tapeworm cysts of sheep communicated to them by dogs. These were found in every flock during the last century. Formerly sheep were kept until they were 3 to 4 years old before they were killed; they then contained hydatid cysts old enough to have developed daughter scolices. Now they are killed at the age of 5 months. Further, during the last 3 decades, the rural population has moved into the towns and villages and one-third of the whole population lives in Reykjavik. *G. Lapage.*

Hartz, P. H. **Human Strongyloidiasis with Internal Autoinfection.** *Arch. Pathology.* 1946, June, v. 41, No. 6, 601–11, 11 figs.

The author describes the infestation of an adult Negro with *Strongyloides stercoralis*. Autopsy was done 40 minutes after death.

He gives a detailed description of the histological changes seen. These cannot be summarized in detail here, but the author emphasizes the almost complete absence of ulceration of the intestinal wall. Only a few microscopic ulcers were seen and these were probably due to the presence of larvae of the nematode in the mucosa. The invasion of the intestinal wall by the larvae was quite independent of this ulceration. In the duodenal wall adult *Strongyloides* were not numerous. Those that were present were found in the stroma of the villi, in the intervillar spaces and rarely in the depths of the crypts of Lieberkühn. In the stroma of the villi there was surprisingly little tissue reaction. The adult nematodes were never surrounded by epithelial sheaths and, although a moderate number of eosinophil cells was present, the eosinophilia was not pronounced. Eggs and the earlier larval phases of the nematode were present only in the epithelium of the crypts of Lieberkühn and villi, never

in the stroma. Often they were present in groups and were completely surrounded by epithelial cells, but there was no desquamation of epithelium and the author considers that the desquamation described by STRONG (*Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases*, 7th Edn. 1944, p. 1278), was due to post-mortem change. Hartz thinks that the eggs and larvae probably stimulate the proliferation of the epithelial cells, so that "incubation chambers" are formed around them. He cannot agree with FAUST (*Arch. Pathology*, 1935, v. 19, 769) that this is a defensive reaction by the host; he thinks, on the contrary, that the epithelial proliferation protects the eggs and larvae. Older larvae had migrated from the epithelium to the crypts of Lieberkühn or to the lumen of the duodenum and were present in great numbers; in the lumen they were never surrounded by epithelial sheaths, but epithelial cells were drawn out and thinned over some of the older migrating larvae. In many places there was marked inflammation in the crypts or at the tips of the villi, rarely combined with fibrinoid necrosis of the tips of the villi. When inflammation of the deeper parts of the duodenal mucosa was present the larvae were found in the lumina of the crypts together with bacteria and leucocytes. Brunner's glands were strongly developed to form large accumulations of glandular tissue and a few eggs or larvae were found in them. Their presence here may have been due to the fact that when the Brunner's glands are strongly hyperplastic, the muscularis mucosae, which is normally a strong barrier against nematodes, may be partly absent.

In the colon the surface epithelium was practically intact and only a few microscopic ulcers were seen. The larvae here were mostly transformed into filariform larvae and had invaded the gut wall, by entering the lumina of the crypts of Lieberkühn, from which they had penetrated the mucosa. Probably these larvae came from the small intestine, because this is the only site in which large numbers of eggs are found. Superficially the mucosa here contained dense infiltrations with plasma cells and eosinophils. In the deeper layers of this part of the alimentary canal many larvae were often present and there were moderate numbers of giant cells and nematodes surrounded by histiocytes or present in small abscesses or without any reaction around them, the eosinophils being few in this region. The submucosal lymphatics of the colon were all dilated and many contained large and small lymphocytes, degenerated neutrophils or eosinophils and erythrocytes. The larvae provoked varying reactions or no reaction at all in the lymphatics. A few larvae were seen in small veins.

In the connective tissue of the submucosa of the colon there were a few intact larvae, but most of them were damaged and had provoked severe reactions. The author emphasizes the formation around many of them of eosinophilic granulomas composed of histiocytes which often formed giant cells by coalescence, lymphocytes, plasma cells and especially large numbers of eosinophils. When the larvae were very numerous the submucosa was studded with these eosinophil granulomas. Larvae had also penetrated into the muscular coats and subserous connective tissue and the intramuscular connective tissue septa, eosinophil granulomatous tissue being formed around these also. There were many granulomas in the subserosa, the mesocolon and mesosigmoid and also in the liver around filariform larvae, which were present either just below the capsule of the liver or deep in its tissue.

The author draws attention to the dilatation of the lymphatics and the presence in them of a "granulomatous lymphangitis" caused by larvae present in their lumina, which led to the encapsulation of the larvae and to more or less complete obliteration of the lumen, with consequent peripheral dilatation. In contrast to filarial lymphangitis, in which oval and more elongated cells predominate [HARTZ, this *Bulletin*, 1944, v. 41, 955], the cells more frequently present in the lymphangitis of strongyloidiasis are large, rounded and

vacuolated histiocytes; later, the contrast between these two conditions is less marked, but nematodes were always present in the granulomas of strongyloidiasis observed in this patient.

The changes observed in the walls of the bowel and in the lymphatics could cause marked functional disturbances, but the subject described was not observed clinically for these. Invasion of the larvae by leucocytes was seen only occasionally, but when the larvae are disintegrating it may occur. [*Cf.* Vinnitzky, this *Bulletin*, 1945, v. 42, 746.] *G. Lapage.*

Henrard, C., Peel, E. & Wanson, M. Quelques localisations de *Wuchereria bancrofti* Cobbold au Congo Belge. Cycle de développement chez *Culex fatigans* Wied, *Anopheles funestus* Giles, *Aedes aegypti* Linnaeus et *Anopheles gambiae* Giles. [**Occurrence of *W. bancrofti* in the Belgian Congo: Development in Mosquitoes.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 212–32. [16 refs.]

The authors publish observations on *W. bancrofti*, both in mosquitoes and man in the Belgian Congo.

The larvae of several nematodes occur in human blood in this region. *W. bancrofti* is not rare, in certain particular localities, and the majority of those infected show no lesions attributable to the parasites: in eighty-seven hydroceles the blood and the hydrocele fluid were negative.

On the entomological side it is shown that *Anopheles funestus* is easily infected in the laboratory, completely so in ten days (temperature not stated). Individual *A. funestus* infected in nature are not rare in houses, and this insect is the normal carrier. The evidence about *A. gambiae* is less full, but indicates that it is probably equally infectable. In *Aëdes aegypti* (contrary to what has been recorded elsewhere) the worm can go through its cycle and reach the labium: it seems that this takes longer in this mosquito than in *A. funestus* and that there is a delayed development of some of the worms. In *Culex fatigans* only a small proportion of larvae go through to the stage found in the labium, and the period in the mosquito seems still more prolonged. This insect is a poor vector, in the Congo. *P. A. Buxton.*

Guyane Française: Rapport sur le Fonctionnement Technique de l'Institut Pasteur de la Guyane Française et du Territoire de l'Inini pendant l'Année 1945 [Floch, H., Director]. (Publication No. 125. 1946. Cayenne.) pp. 90–99. [20 refs.] Filariose à *W. bancrofti*. [**Filariasis associated with *W. bancrofti*.**]

Records of the prevalence of *Mf. bancrofti* in the blood of residents in Cayenne have varied greatly. Thézé in 1916 found 37 among 103 examined, and three with embryos of *F. demarquayi*; Tisseuil in 1934 found 24 per cent. positive [number examined not stated] and a year later 12 per cent. among hospital patients, and 18·6 per cent. of 240 examined at the institute of Hygiene. In Martinique, Noc and Stévenel reported 5·47 per cent., Low 32·8 per cent. in St. Kitts; Flu 3–60 per cent. in Dutch Guiana according to social standing; at Belem, Brazil, Causey *et al.* reported in 1945 that 10 per cent. of 5,000 persons examined were carriers of *W. bancrofti*.

In 1944–45 in Cayenne the blood of 683 persons was examined by smear and by thick drop between the hours of 3 and 10. Of the totals 430 were Creoles and the remaining 253 included Senegalese, Arabs, Asiatics and Europeans; of the Creoles 320 were males, 110 were females; 12·1 per cent. of the former and 18·1 per cent. of the latter were positive. The ages of highest infestation

were 21–30 in men, 31–40 in women. Several species of mosquitoes were examined, but *C. fatigans* appears to be the sole vector in French Guiana, 11 per cent. of 1,113 specimens being positive.

The question of lymphangitis, elephantiasis and *W. bancrofti* infestation was also studied. Of 430 persons examined 31 had, or had recently had, lymphangitis and six, or 19 per cent., of them were harbouring *W. bancrofti*, whereas of 399 without lymphangitis 52, or 13 per cent., showed microfilariae. The evidence in favour of the microfilarial origin of the lymphangitis is, therefore, not very strong and the clinical signs—abrupt onset with fever and local inflammation, systemic disturbance, at times suppuration yielding to sulphonamides—are all in favour of a bacterial (streptococcal) cause. The Dick reaction was tested in 204 subjects; 16 per cent. of those who had had "lymphangitic crises" and 11 per cent. of those who had not gave a positive result, but of four during such a crisis and ten elephantiasis patients none reacted positively. This immunity, it is said, disappears rapidly after the crisis, but the organism remains latent until it again gives rise to another crisis. The case is cited of a woman who in 1939 started to have attacks of lymphangitis which necessitated her keeping in bed for as long as a fortnight; these attacks occurred practically every month at first and later they became more frequent. Various forms of treatment had been tried but ineffectually until she was given a vaccine, "antilymphangitic streptococcal". After 10 injections the crises ceased and the oedema subsided.

The question of elephantiasis being dependent on filariasis in warm countries is also considered. At Belem, among 4,936 non-elephantiasis persons 535 were harbouring filariae (10·8 per cent.) and of 64 elephantiasis patients there were six with filaria (9·4 per cent.). At Cayenne, of 59 with filariasis three had elephantiasis (5 per cent.) and among 371 without filaria [this presumably means "in whose blood embryos were not found"] 17 had elephantiasis (4·5 per cent.). This is interpreted as implying that the percentage of elephantiasis patients and those without elephantiasis harbouring the embryos of *W. bancrofti* are about the same in number. Brumpt is quoted as saying that of 100 persons with microfilariae two to five run a chance of developing elephantiasis, but the report goes on to say that the same may be noted of those without filaria, which is equivalent to saying that the presence or absence of nocturnal microfilariae and of elephantiasis is no more than a coincidence.

Finally, mention is made of authors such as Manson, Le Dantec and Dufougeré, who maintain, or believe, that a primary filariasis and a secondary bacterial infection set up elephantiasis, and the report concludes that elephantiasis is a common complication of chronic streptococcal infection, but each may evolve independently. "Tropical lymphangitis ought not to be regarded as a mere complication (pousée) of elephantiasis; it merits a place by itself as a separate affection". *H. Harold Scott.*

PRATT, I. & NEWTON, W. L. **The Migration of Infective Larvae of *Wuchereria bancrofti* within the Mosquito Host and their Rate of Escape under Laboratory Conditions.** *J. Parasitology.* 1946, June, v. 32, No. 3, 272–80, 2 figs.

After a study of the literature the authors found that the migration of the infective larvae of *Wuchereria bancrofti* in the mosquito vector has been the subject of only incidental observations and that there is no statistical verification of the view that their escape from the mosquito is necessarily associated with the taking of blood meals by the mosquito. They quote the work of several authors, which indicates that about two weeks must pass while the

larvae are in the mosquito before they become infective, and that they then pass first to the abdomen and from there migrate through the thorax to the head and proboscis and that the infective larvae may emerge apart from blood meals, either when pressure or heat is applied or when the mosquito feeds upon sugar solution.

The authors themselves allowed *Culex quinquefasciatus* [*C. fatigans*] to feed at night upon a subject infested with the periodic strain of *W. bancrofti*. Three lots of mosquitoes were used, each lot containing about 75 to 100 females; and three separate feeds were allowed. The females were allowed access to the subject's arm between 11 p.m. and 5 a.m. Examination of the finger-tip blood between 11 and 12 p.m. usually showed 20 to 30 microfilarial larvae per 20 cm. of blood. The gorged mosquitoes were put in cages at a temperature of 74° to 80°F. and a relative humidity of 75 to 85 per cent., and were supplied with sugar solution on cotton pads. Earlier experiments had shown that the larvae usually reach the infective stage at the end of 16½ days under these conditions. At the end of this 16½-day period and at intervals, of 2 days until 30½ days, and again after 39½ days, the mosquitoes were killed and the proboscis, head, thorax and abdomen were dissected separately; the infective larvae were counted in each of these parts of the mosquitoes. The earlier dissections revealed many larvae in the thorax, which had not reached the infective stage, and, when these were normal and motile, they were counted as potential infective larvae. Table 1 shows the results of the dissection of 209 mosquitoes.

The average numbers of larvae found per mosquito at the different intervals were: 48·7 at 16½ days; 43·1 at 18½ days; 30·0 at 20½ days; 20·2 at 22½ days; 13·6 at 24½ days; 11·6 at 26½ days; 10·2 at 28½ days; 8·8 at 30½ days and 1·5 at 39½ days (in 6 mosquitoes still alive then). Thus, during the 14 days between 16½ and 30½ the decrease of the average number of larvae per mosquito was from 48·7 to 8·8, the loss indicating the number of larvae which had left the mosquitoes by the proboscis (see below). The loss was not statistically significant until after 18½ days. There was considerable variation in the number of larvae found in the different mosquitoes, and the authors explain this difference by experimental factors which they could not control; they could not determine, for example, the relation between the time of the feeds taken from the subject and the maximum concentration of microfilariae in the subject's blood, and there is some evidence that individual larvae need variable times to become infective or migratory, some of them requiring longer than 16½ days and some becoming infective before that time. Statistical analysis showed, however, that the average numbers given by the authors were stable.

The figures given of the average numbers of larvae found in the different parts of the mosquitoes indicate that at 16½ days there was considerable migration from the thoracic muscles to the abdomen. Two days later, the thorax was still losing larvae, but the larvae were also leaving the abdomen for the head and proboscis. This process went on for 4 days or longer; but, although the thorax and abdomen were losing larvae fairly rapidly during this time, the head and proboscis were not gaining them after 18½ days. The authors conclude that, after 18½ days, the larvae were probably escaping from the proboscis. The reasons for this conclusion are discussed. Among them is the authors' observation that larvae did emerge when the anterior end of the proboscis was immersed in saline without any other stimulus, and that spontaneous emergence often occurred when the proboscis contained five larvae or more. Eight or ten larvae would emerge within a minute. The authors also found evidence of the rupture of the proboscis, and the larvae were never seen to emerge from any other part of the body. No larvae were found on the cotton pads soaked in sugar solution, on which the mosquitoes were fed, but the authors concluded

that they escaped while the mosquitoes fed on this solution; or when the proboscis was ruptured because it was too tightly packed with larvae.

The figures also show that there was a continued rapid migration of larvae from the thorax and abdomen to the proboscis after 18½ days.

Most of the larvae had left the mosquitoes by 24½ days and those that were left at that time seemed to migrate back and forth from the abdomen to the head, a few occasionally leaving the proboscis; but so few larvae were then present that accurate conclusions on this point could not be drawn.

Under natural conditions loss of larvae can be expected during the week after they reach the infective stage. *G. Lapage.*

WHARTON, D. R. A. **Transplantation of Adult Filarial Worms,** ***Litomosoides carinii*****, in Cotton Rats.** *Science.* 1946, July 12, 30–31.

Pointing out that the experimental study of filariasis is handicapped by the prolonged period required for the development of the adult in the definitive host, and by the difficulty of observing this phase of the life-history, the author tried to overcome this difficulty by transplanting adult specimens of *Litomosoides carinii*, parasitic in the cotton rat, *Sigmodon hispidus*, into normal, uninfected cotton rats.

The infected cotton rats were anaesthetized with ether, the thorax was shaved and the body was swabbed with "a solution of phenol", the thoracic area being washed with alcohol. "A slit" was made with scissors along the anterior midline and continued along the sternum up to the clavicle. The sides were pinned down to expose the pleural cavities, and the nematodes were withdrawn from these aseptically with forceps or, better, with "a hooked rod." They were then placed in sterile saline. The rat into which they were to be transplanted was anaesthetized with ether, shaved and swabbed and then the central area of the "right anterior thorax" was punctured with a thin blade, the opening being kept open with blunt hooks to make possible the insertion, with the aid of a blunt probe, of 5 to 25 specimens of *L. carinii*.

Attempts to transplant this species of nematode into 10 normal cotton rats have so far failed. As early as three days after the transplantation the nematodes are dead and are accumulated in a single mass which becomes a "syncytium of degenerating worms." Living microfilariae may, however, be found for a week or longer in the pleural cavity and in the blood. There was no gross exudation of fluid into the pleural cavity, which appeared to be healthy, the "syncytium of worms" being cleanly isolated in a serous covering.

Successful transplantation was, however, accomplished into splenectomized cotton rats, the reticulo-endothelial system of these latter having previously been blocked with Indian ink. Variable numbers of living *L. carinii* were recovered from the pleural cavity of 4 out of 9 rats used, and there were indications that the nematodes in one other rat had lived long enough to migrate from the right to the left pleural cavity. The males often survived effects of the defence mechanism of the host which killed the females. The exudations of the females seemed to be more irritating than those of the males. Nematodes transplanted into one side of the thorax were later found in approximately equal numbers in the pleural cavities of both sides and can migrate across the mediastinum, through the fatty tissues or between the parietal pleura and the diaphragm. The author found the nematodes in these tissues.

Successful transplantation into two out of three rats has also been accomplished after these rats had been treated by "X-irradiation with 140 kv. 5 M.A. (without filters) at 25 cm., using a large cone (over 7 cm.) and delivering

120 r. per minute." The type of cell and tissue most affected by this treatment, as contrasted with that of blockade, offers significant data about the resistance of the host.

Successful transplantation has also been effected from one naturally infected rat to another naturally infected one. Also rats injected four or five times during as many weeks with a suspension of *Dirofilaria immitis* in a mixture of Falba, mineral oil and killed tubercle bacilli [see FREUND and BONANTO, *Bulletin of Hygiene*, 1945, v. 20, 162] have "accommodated transplants" of living specimens of *L. carinii* and in one of them "lymph node invasion" was observed. More details of the pathological observations will be published later. SCOTT and CROSS (*J. Parasitology*, 1945, v. 31, Supp., 15) noted in old cotton rats tumours in the superior mediastinum which were, they assumed, caused by the dead adult filarial nematodes. Wharton has also "not infrequently" observed tumours which are the result of the death of the nematodes while they are in transit through the fatty lymphoid tissue in the superior mediastinum near the hilum of the lung. He considers that this is accidental. A characteristic feature of the infection is, however, a generalized or spotty proliferative reaction of the visceral and parietal pleura, which culminates in papillary nodulations on its surface. Neither the nematodes nor the nodules invade the lung proper, although the lung shows a reaction to the infection. The spleen is hypertrophied. *G. Lapage.*

FRANKS, M. B. **Blood Agglutinins in Filariasis.** *Proc. Soc. Exper. Biol. & Med.* 1946, May, v. 62, No. 1, 17–18.

FRANKS, CHENOWETH and STOLL (*Amer. J. Trop. Med.*, 1946, in the press) have studied, on Okinawa island, the frequency distribution of the A, B blood groups. The blood group percentages of 1,000 persons (about 5 per cent. of the population) were compared with the frequency distribution of the A, B blood groups of 180 persons from the same villages whose circulating blood contained microfilariae. The number of microfilariae was determined by dilution counts.

A table shows that the incidence of filaraemia is greater among persons whose sera contain no natural antibody to group A red cells.

The results are shown below :—

TABLE I

Frequences of the A, B Blood Groups in Persons with Microfilaraemia compared with the Systematic variations in the Frequencies of the Blood Groups on Okinawa.

	A	AB	O	B
Percentage in 1,000 Okinawans*	40·8	8·3	31·8	19·1
Percentage in 180 persons with filaraemia	52·0	10·3	25·9	11·8
†Statistical significance of differences	Significant	Not significant	Possibly significant	Significant

* Comdr. Fink has since done 500 additional typings from these villages without any appreciable change in percentages given here.

† The odds against the occurrence of the differences in the ratios arising by chance alone are approximately 40 to 1 for A, 1 to 1 for AB, 10 to 1 for O, and 140 to 1 for B.

The author remarks that the data here given are not sufficient to determine the immunological significance of the presence of isoagglutinins in five sera from filarial patients, and that there is at present no support for the attractive hypothesis that the agglutinin is produced as a result of stimulation by a

substance present in the filarial nematode, which resembles a blood group substance. The evidence available suggests that further work on this subject is required. *G. Lapage.*

SAUNDERS, G. M., BIANCO, A. A. & JORDAN, W. S. **Intradermal Tests with "Dirofilaria immitis" Antigen as a Diagnostic Aid in Human Filariasis.** *U.S. Nav. Med. Bull.* 1946, Aug., v. 46, No. 8, 1242–53. [12 refs.]

The authors summarize in some detail the results of earlier workers, most of which have been recorded in this *Bulletin*. Their own observations were made upon three groups of male patients in the United States Naval Hospital, Bethesda, Md. Group 1 consisted of 117 subjects with a clinical diagnosis of filariasis. Further examination established this diagnosis in most of them, but the diagnosis of some remained doubtful. Group 2 consisted of 155 without a clinical diagnosis of filariasis, but with a history of exposure to infestation in the Pacific area. Group 3 consisted of 117 who had never lived in areas in which filariasis is known to be endemic ; they were being treated for gastro-intestinal complaints, allergies or "pulmonary disease". The antigen used was a dilution of 1:10,000 of a saline extract of dried *Dirofilaria immitis* made by the method of BOZICEVICH and HUTTER [this *Bulletin*, 1944, v. 41, 1055].

No "control antigens" were used. After injection of 0·1 cc. of the antigen into the flexor surface of one forearm, the reaction was read after 10 minutes and 24 hours. The result was regarded as positive if a weal with a surrounding erythema developed within 10 minutes (immediate reaction) or if there was, within 24 hours, an area of erythema with a diameter greater than 1·5 cm. with subcutaneous oedema (delayed reaction). The authors followed the interpretations used by King [this *Bulletin*, 1945, v. 42, 304].

The results are shown below :—

Results of skin tests with 0·1 *cc. of* 1:10,000 D. immitis *antigen*

Reaction	Patients with diagnosis of filariasis		Patients exposed to filariasis		Patients without known exposure	
	Number	Per cent.	Number	Per cent.	Number	Per cent.
2 to 4 plus immediate ...	80	68·4	38	24·5	11	9·4
0–1 plus immediate 2–4 plus delayed	4	3·4	4	2·6	0	0
Total with 2 to 4 plus ...	84	71·8	42	27·1	11	9·4
Total with no reading more than 1 plus ...	33	28·2	113	72·9	106	90·6
Total	117	100·0	155	100·0	117	100·0

When all 2-plus reactions (with a weal and erythema but without pseudopods) were excluded, the positive reactions in the three groups were : group 1, 59 per cent. ; group 2, 20 per cent. ; group 3, "about" 4 per cent. Delayed reactions were thus not common. Only a few developed painful rubbery swelling of the arm, and in only a few did oedema developing after 24 hours persist longer than 2 to 3 days. None showed generalized reactions or exacerbation of the filariasis. A special analysis was made of the results given by 23 subjects of group 1 who had the most definite signs of filariasis, *e.g.*, acute lymphangitis

of the extremities or of the spermatic cords, or circumscribed soft tissue swellings, or epitrochlear, axillary or postcervical adenopathy, or soft tissue calcifications demonstrated by X-ray, or microfilariae in the blood. Skin tests were positive in 22 of these 23. Allergic conditions (hay fever, asthma, hives) were present in 30 of the 117 in group 3, but only one of these 30 (who had a history of hives) gave a positive skin reaction. The authors say that this result agrees with those obtained by BOZICEVICH and HUTTER.

The possible influence of other species of nematodes parasitic in the intestine was investigated. The authors do not, however, consider that the figures in group 1 are high enough to be statistically significant. The stools of 141 subjects of group 2 were examined and those of 22 contained eggs of hookworm (in 19) and *Trichuris* (in 3). Of these 22, six gave positive skin tests. Of the 119 subjects whose stools were negative 28 gave positive skin tests while 81 did not. [There seems to be a discrepancy here; the text gives these figures, but 28 plus 81=109 not 119]. The stools of 84 of the 117 in group 3 were examined, but those of two only contained eggs, these being eggs of hookworm in both instances. Both gave positive skin tests. The authors also examined 17 patients infested with hookworm or *Trichuris* [presumably these did not belong to any of the 3 groups already mentioned] and concluded that there did not seem to be any difference between the sensitivity to *D. immitis* antigen of those with or without "intestinal worms". The experience of the authors agrees with that of COGGESHALL (*Amer. J. Trop. Med.*, 1945, v. 25, 177) [apparently this is the reference meant], who concluded that 96 per cent. of a large series of individuals suffering from filariasis had been in the Samoan group of islands, while only 4 per cent. of them had been elsewhere. In group 1 of the present authors' subjects positive reactions were given by 81·5 per cent. of those who had been in the Samoan area and by only 45·5 per cent. of those who had been exposed elsewhere. Of those in group 2, 40 per cent. of those who had been exposed in the Samoan area gave positive skin tests, while these were given by only 25 per cent. of those exposed elsewhere.

The percentage of eosinophils was considerably higher in persons with filariasis and moderately higher in group 2 than in group 3. Eosinophil counts above 5 per cent. were found in 37 per cent. of group 1, 16 per cent. of group 2, and 5 per cent. of group 3. These differences may have been partly due to heavier infestations with intestinal "worms" in subjects with service overseas; but, when eosinophil counts were done on those whose stools revealed no helminth eggs, more than 5 per cent. of cosinophils were found in 18·5 per cent. of 27 subjects of group 1, in 12 per cent. of 108 in group 2, and in 5 per cent. of 101 in group 3. Further, the percentage of eosinophils in those giving positive skin tests was greater than it was in those giving negative skin tests, whether these belonged to group 1 or group 2.

The authors conclude that the use of larger amounts of antigen offers no advantage and may cause severe reactions and an increased number of false positives. Different workers have interpreted the results differently, but a weal surrounded by erythema developing in 10 minutes, whatever its size and whether pseudopods, oedema or a delayed reaction develop or not, may be regarded as a positive. Apparently infestation with any of the *Filariidae* will produce such a reaction. The presence of positive reactions to *D. immitis* antigen and also to dog protein, *Trichinella* antigen or *Ascaris* antigen does not necessarily mean that these antigens have a common factor, because a few subjects are recorded who gave positive reactions to these antigens but not to that of *D. immitis*. There is little evidence that infestation with nematodes other than *Filariidae* will produce sensitivity to *D. immitis* antigen. It should be remembered that an unknown exposure to *Wuchereria bancrofti* may have occurred, because this species is endemic in the southern United

States. Thus STRONG (*Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases*, 1943, 6th edn. p. 1298) reports that, in 1919, in Charleston S.C., 77 (nearly 20 per cent.) of 400 subjects examined had circulating microfilariae in their blood and that cases of filariasis had been found as far north as Washington, D.C.

The general conclusion of the authors is that skin tests done with *D. immitis* antigen are " doubtless a valuable aid " to diagnosis and may be " highly specific ". *G. Lapage.*

MADSEN, H. **Biological Observations upon** *Enterobius vermicularis* **(Pinworm).** Reprinted from *Acta Path. et Microb. Scandinavica.* 1945, v. 22, No. 4, 392–7. [21 refs.]

The author discusses his reasons for concluding that infestation with *Enterobius vermicularis* occurs most often by inhalation of the embryonated eggs rather than by contamination of the finger nails and communication of the eggs to the mouth [see also SCHÜFFNER, this *Bulletin*, 1946, v. 43, 233].

Discussing the migration of the female *Enterobius* down to the rectum, the author rejects the theory of KOCH (*Zent. f. Bakt.*, I. Abt. Orig., 1925, v. 94, 208) that, when the females are full of eggs, the oesophageal bulb is pushed aside by the gravid uterus, so that the female is forced to release her hold on the wall of the small intestine and is forced down the intestine by peristalsis to the rectum and then creeps out of the anus " by chance " and cannot find her way back again. LANGHANS (*Arch. f. Kinderheilk.*, 1926, v. 77, 27) noted that the oesophageal bulb of females which had just emerged from the anus functioned at maximal capacity although the uterus was full of eggs, and the author himself obtained from the lower part of the colon by means of enemata, plenty of " both pregnant and quite small females " and also males, during a period of 2 weeks, although the faeces during the same period contained only a few of the nematodes. Madsen concluded that males and females can remain in the lower part of the colon and in the rectum. The eggs which he obtained from females by enemata did not embryonate, while those obtained from females from the rectum more often did so. Eggs taken from females which had emerged " spontaneously ", on the other hand, practically never failed to embryonate. The author concludes that the maturation of the eggs, rather than any mechanical factor, determines the migration out of the anus. He claims that this view is confirmed by the observations of LEUCKART (*Die menschlichen Parasiten*, 1876, 2. Bd. I–IV, pp. 1–882) that females spontaneously emerging from the anus seldom contain eggs which are in their earlier phases of development, most of them having exhausted and fatty ovaries.

Madsen also often found, by the pestle method of SCHÜFFNER and SWELLENGREBEL [this *Bulletin*, 1945, v. 42, 922 and 924] which takes material from the perianal skin, females empty or almost empty of eggs, and concluded that the female can move out of the anus and in again in order to lay the eggs in batches and that the males can also wander in and out in this way. The periodicity of this emergence is often monthly, and the author suggests that it is so because the period of development of the nematode is 4 or 5 weeks. This view is supported by the work of HEUBNER (*Jahrb. f. Kinderheilk.*, 1922, v. 98, 1) on this author's own infestation, and that of DESCHIENS (*Presse Méd.*, 1935, v. 43, 404) on *Enterobius anthropopitheci* in a chimpanzee. This explanation is more likely than the view that a development of the nematode larval phases takes place in the intestinal tract of the host, especially in the caecum. ZAWADOWSKY and SCHALIMOW (*Ztschr. f. Parasitenk.*, 1930, v. 2, 12) showed that the eggs of *E. vermicularis* must have reached the tadpole stage before they can develop outside the host and that they then require oxygen. Further, the eggs are

regularly laid " in the anus " and not in the intestine of the host and are not mature until the nematodes are leaving the intestine. Even the eggs which may, as MADSEN (*Bibl. Laeger.*, 1941, No. 5, p. 113) showed, have been found in the intestinal wall and could there obtain oxygen from the host's blood, never developed to the tadpole stage. This hypothesis of the development of the nematode in the host's intestine is contrary to our knowledge of the development of nematodes related to *Enterobius*, and should be abandoned for ever. *G. Lapage.*

BIJLMER, J. **An Exceptional Case of Oxyuriasis of the Intestinal Wall.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 359–66, 11 figs. [20 refs.]

Bijlmer makes a unique contribution to the literature of oxyuriasis by describing a remarkable case of invasion of the intestinal wall, particularly of the rectum, colon and ileum, by thousands of immature *Enterobius vermicularis*.

The patient, a man of 46 years of age, suffered for the last six months of his life from diarrhoea. This grew so violent that on admission to hospital he was already moribund and was passing from 10 to 12 watery stools, with blood, daily. Bacteriological and serological tests were negative. At post mortem there was gangrenous ulceration in the rectum, colon and ileum. The submucosa and subserosa were penetrated by numerous oxyurids. The worms were spread evenly throughout the intestinal wall but in places they were aggregated in large numbers. In an 11 cm. square of rectum there were more than 650 immature worms, of which about 200 were lying transmuscularly. The total number of worms present in the intestinal wall alone was estimated at over 10,000. The proportion of males to females averaged 5 to 1 in the colon and 6 to 1 in the rectum. All were very small. The males averaged 1,550μ, the females ranged from 1,200μ to 2,325μ, none contained eggs.

Evidence was obtained that the worms pass into lymph vessels and even into large blood vessels.

Bijlmer is of opinion that the ulcers, which had undermined edges, were invaded secondarily and were not primarily caused by the worms. There was no noticeable inflammation in the neighbourhood of the parasites.

The contents of this communication have already appeared in 1944 in Dutch (*Nederl. Tijdschr. v. Geneesk*, 1944, Jan. 8, v. 88, Nos. 1/2, 24) in substantially the same form with ten figures. The additional figure accompanying the present paper illustrates the male spicule. *R. T. Leiper.*

WIRD, K. **A Trichinosis Epidemic in the Borås District, its Clinical and Epidemiological Aspects.** *Acta Med. Scandinavica.* 1946, Oct. 15, v. 126, No. 1, 1–16. [Numerous refs.]

Trichiniasis is a relatively rare disease in Sweden. In some years no case is seen, in others half a dozen or so ; larger outbreaks have occurred in 1917 (18 cases), in 1937 (about 50 cases), in 1944 in the Alingsås district (13 cases), and in October of the same year the one recorded in this paper, 37 cases in Sparsör, 6 kilometres from Borås. The cases were typical as regards signs and symptoms ; nearly all had facial swelling, with nausea, vomiting, diarrhoea, fever, headache and eosinophilia.

Investigation revealed that all had eaten pork from one ham-and-beef shop, the proprietor of which obtained all his pork from one source, a butcher who supplied all the shops in Borås once a week. Nine farmers supplied him with pigs and the infested pig was traced to one of these ; but how this pig became infested remained an unsolved problem.

Of the 37 patients 35 gave a positive precipitin reaction ; two refused to be tested, but they were clinically typical. Of the total 17 were women, 20 were men ; the former " tasted " the raw force-meat or sausage-meat for seasoning, the latter ate raw smoked ham and sausage. The incubation period was determined in six cases and ranged between 14 and 24 days. Linneweh in 1943, from a study of 60 cases, found the average in 24 mild cases was 14 days, in 10 moderate cases 11 days, in 26 severe cases 7 days. Michaelis in 1940 found it to range from 13 to 39 days, usually 18–23, and Sylla in 1942 in 117 cases found it to range between 8 and 30 days. In general, the more severe the case the shorter is the incubation period. It is not always easy to determine the earliest symptom, as the onset may be vague, but in the majority (35 out of the 37 in this outbreak) oedema of the eyelids is the first sign noticed. Leucocytosis ranged between 10,000 and 29,000 per cmm. and eosinophilia from 6 to 72 per cent., but, as others have also found, there is no relation between the degree of eosinophilia and severity of the disease ; in fact, in the very severe it may be low. Faecal examinations were made for the worm and blood examinations for the larval forms, but none was positive. Skin tests with *Trichinella* antigen were positive in 25 out of 34 patients, but were negative in some with typical clinical symptoms. Fouadin is said to be beneficial in treatment, but none was obtainable ; those patients with fever were given sulphathiazole, but without benefit.

Seven to 8 months later, 24 persons returned for re-examination ; four still had slight muscular discomfort and ready fatigue, none of the others had any complaint. None had eosinophilia above 4 per cent., and one who had had 72 per cent. now had only 1 per cent.

Another case occurred in the same district 9 months later. It was quite typical and the infested pig was traced ; the incubation period in this case was 16 days. *H. Harold Scott.*

Roth, H. **Employment of Serological and Skin Tests at Outbreaks of Trichinosis in the Alingsås and Borås Districts (Sweden).** *Acta Med. Scandinavica.* 1946, Oct. 15, v. 126, No. 1, 17–33, 1 fig. [Numerous refs.]

Serological and skin tests are of greater value for diagnosis than the more direct methods of looking for worms in the faeces, or for larvae in the blood stream, or in muscle biopsy. The immunological tests mentioned by the author are five in number :—(1) Bachman's intradermal test [see this *Bulletin*, 1928, v. 25, 963 ; 1929, v. 26, 551 ; 1933, v. 30, 694 ; 1934, v. 31, 395, 802 ; 1937, v. 34, 458 ; 1939, v. 36, 146, 847 ; 1945, v. 42, 55]. (2) Bachman's serum precipitin test [see this *Bulletin*, 1928, v. 25, 470 ; 1930, v. 27, 980 ; 1942, v. 39, 194, 196]. (3) Complement fixation with *Trichinella* antigen, Gaase *et al.* [see this *Bulletin*, 1930, v. 27, 981 ; 1943, v. 40, 478 ; 1946, v. 43, 236]. (4) Microscopic flocculation slide test of Suessenguth and Kline [see this *Bulletin*, 1946, v. 43, 359, 360]. (5) Microscopic precipitin test, carried out by placing living *Trichinella* larvae, artificially digested to free them from their capsules, in serum. Immune serum (perhaps the euglobulin fraction) gives this precipitate. The technique is fully described by the author ; those interested should consult the original : it is too detailed for transcription here.

In the Alingsås epidemic, 31 samples of blood were obtained from 16 possibly infested persons ; 13 were positive by this last test, the " living trichinae precipitin test ", as the author calls it ; 12 of the 13 were clinically typical. Intradermal tests were carried out on 12 of the serologically positive and 2 of the negative, but these are not comparable because various antigen dilutions were used and differing reading times.

In the Borås epidemic, 80 samples of blood were obtained from 45 suspected patients, and 9 months later 4 samples from two others living on a farm where trichinosed meat had been eaten. Positive results were given by the sera of 36 who had presented typical symptoms. The 11 negative had been ill with indefinite symptoms, by no means typical, hardly even suggestive, of trichiniasis. The times when positive findings were observed are worth noting: Of 17 samples tested within the first 10 days of illness only 3 were positive; of 24 during the second 10 days 23 were positive; of 27 taken between the 21st and 70th days all were positive. Of the 36 reacting positively, 26 were tested by the Bachman precipitation test and 25 reacted. [Later it is stated that "Practically all patients suspected in connection with the trichinosis epidemic were submitted to one or more intradermal skin tests with antigen dilutions 1 : 10,000, 1 : 2,000 or 1 : 1,000. The outcome was not always quite uniform, not even in the same patient. . . . Altogether 25 of these patients gave a positive reaction, which in 17 appeared as the characteristic immediate reaction with enlargement of the injection papules and, in most cases, with formation of a broad zone of erythema, so that the redness could still be demonstrated after 24 hours. In 8 cases the reaction was only slightly positive, mostly in the form of a delayed reaction after 24 hours. In 5 cases the reaction was considered dubious—in 2 of these patients the reaction to the simultaneous control injection with saline was just as strong as that with the antigen. Finally, 4 patients were entirely negative."] Re-examination 7–8 months later showed that the antibody content had considerably diminished, but was still demonstrable and then gradually faded, persisting longest, it would seem, in those most heavily infested.

In some cases the dermal reaction appeared earlier than the serological, but the results were too inconsistent for any valid deductions to be drawn.

The author concludes that the intradermal test did "not quite come up to the great expectations suggested by most of the reports in the literature," and that the new microscopical precipitin test with living larvae is the most sensitive and specific. [A paper of great interest.] *H. Harold Scott.*

MOOREHEAD, M. T. **Roentgen Therapy and Trichiniasis: Report of Unusual Case of Trichiniasis treated with Apparent Success by Irradiation with Study of Quality of X-Rays used and Review of Subject.** *Maine Med. Ass. J.* Portland. 1946, June, v. 37, 141. [Summary taken from *J. Amer. Med. Ass.* 1946, Aug. 31, v. 131, No. 18, 1533.]

Moorehead reports a case which was noteworthy because of the appearance of a sizable extrathoracic tumor mass late in the course of an undiagnosed severe infection by Trichinella spiralis in a man aged 44, a Filipino. This mass had the external appearance of sarcoma but at operation proved to be trichinous. After operation a severe suppurative condition of the chest wall developed at the operative site. This failed to heal despite months of varied treatment and eventually became a serious threat to the patient's life. Complete recovery took place with surprising rapidity following the use of roentgen therapy. The total amount of X-radiation given the patient was approximately 500 roentgens as measured in air. This seems to be the first report of a tumor-like trichinous lesion and also the first instance of the successful use of roentgen rays in the treatment of trichiniasis.

DEFICIENCY DISEASES.

BURGESS, R. C. **Deficiency Diseases in Prisoners-of-War at Changi, Singapore, February, 1942, to August, 1945.** *Lancet.* 1946, Sept. 21, 411–18, 2 figs. [11 refs.]

About 52,000 British troops were interned by the Japanese in Changi Camp, Singapore, in February 1942. Dr. Burgess describes the state of nutrition of these prisoners during 3 years and 8 months of their internment. For nutritional purposes it may be divided into 3 periods :—the first four or five months when the diets were inadequate in calories and the vitamins of the B complex ; the second of nearly 3 years when the diets were more or less adequate ; and the third period (the last six months or so) when the diets were grossly inadequate in calories and contained less than minimal requirements of the vitamin B complex.

Throughout the whole time there was ample vitamin A value in the diets derived from the carotenes of red palm oil and green leaves. Also there was sufficient vitamin C supplied in roots and leaves. Sprats and dried fish supplied adequate calcium and phosphorus.

A sufficiency or otherwise of vitamin B_1 is generally estimated in reference to the non-fat calories of the diet. Unfortunately all authors are not in agreement on the quantities of vitamin B_1 in various foodstuffs. In correlating the outbreaks of beriberi in the camp with the amount of this vitamin in the diet Dr. Burgess uses two tables—that of PLATT and that of WILLIAMS and SPIES. The latter give lower values than the former.

Beriberi appeared in six weeks on a daily intake of 0·39 mgm. (0·2 mgm. per 1,000 non-fat calories (N.F.C.)) ; there were no fresh cases when the intake rose to 1·2 mgm. (0·5 mgm. per 1,000 N.F.C.) : a further outbreak occurred on a daily intake of 0·9 mgm. (0·36 mgm. per 1,000 N.F.C.). These estimates are based on Platt's tables.

The author states that 0·4 mgm. per 1,000 N.F.C. is " probably the minimum " needed to prevent cases of beriberi appearing in a large group. The figure is about 0·3 mgm. per 1,000 N.F.C. using the lower level tables of Williams and Spies.

During the early months there were cases of the encephalopathy of Wernicke. " Treatment and prophylaxis with vitamin B_1 were eminently satisfactory." During the last months when the protein intake fell to 40 gm. daily per person there were many cases of nutritional oedema which complicated the diagnosis of beriberi.

The conditions which appeared when the riboflavin level in the diets was low were :—angular stomatitis, glossitis, palatal erythema, scrotal dermatitis, aching feet, keratitis, retrobulbar neuritis and nerve deafness. These signs appeared in 80 days on an intake of 0·21–0·25 mgm. of riboflavin per 1,000 calories, persisted on a level of 0·35 mgm. and the outbreak did not end until the level reached 0·5 mgm. per 1,000 calories.

During the first 18 months of the internment there were 40 cases of spastic paraplegia.

The occurrence of a pellagroid skin rash had some relationship to a low intake of niacin.

The incidence of the signs of riboflavin deficiency was less among those recruited for labour under conditions of starvation and appalling hardship when 44 per cent. died. Dr. Burgess states :—" When a man is consuming his own tissues his need for riboflavin may be less ", and again :—" The impression gained was that riboflavin deficiency was essentially a disease of the man who was maintaining or gaining weight." [There is, however, another interpretation,

namely that there may be extreme deficiency gravely affecting the metabolic processes of the body without any particular manifestations, such as the mouth and skin signs, appearing.]

During the first year 80 per cent. of the prisoners suffered from bacillary dysentery, usually in a mild form; later amoebic dysentery occurred and became increasingly common. The camp was free from malaria until the last 18 months and then 70 per cent. of the prisoners became infected.

[This paper by Dr. Burgess and other papers by others who have done similar devoted work in the prison camps of the Far East are a great contribution to present-day knowledge of human nutrition.] *L. Nicholls.*

Jörg, M. & Aguirre, J. A. Investigaciones sobre enfermedades Carenciales. Expresión radiológica de alteraciones intestinales en hipovitaminosis B y estados de desnutrición en el hombre. [**Deficiency Diseases. Radiology of the Intestine in Vitamin B Deficiency and States of Undernourishment in Man.**] *Universidad Buenos Aires: Misión de Estudios de Patologia Regional Argentina (Jujuy.). Publicación No. 72.* 1946, 68 pp., 60 figs. [41 refs.]

The authors state that there are three factors essentially dietetic, which may lead to deficiency of the vitamin B complex: (1) Consumption of bread and other foods made with white flour; (2) prolonged cooking of vegetables and addition of alkalies, bicarbonate of soda, baking powder, etc.; (3) excessive consumption of carbohydrates. They describe in minute detail the morbid anatomy and histology and anomalies of secretion of the small intestine in conditions of vitamin B deficiencies, especially of thiamin, and present X-ray pictures of the changes in motility and muscular tone of the bowel and the production of the "wax mould", "accordion", "fragmentation" and "fish skeleton" appearances from localized pocketing and stagnation of contents. These changes, of course, are not specific for avitaminosis B. Brief notes are given of six cases, patients who for one cause or another had subsisted for a long time on a restricted diet.

Probably the most interesting section of the article is that describing the morbid histology of the intestine, and the alterations in the nerves of Auerbach's plexus, notably neurofibrillosis and disintegration of the fibrils, nodular swelling of them and of the axis cylinders of the ganglion cells. Various stages of degeneration may be seen; simple fusiform or nodular swellings with oedema of the neuroplasm and dissociation of the fibrils. These changes are well shown by photomicrographs of tissue stained by Cajal's method. *H. Harold Scott.*

Brennan, D. J. **The Burning Feet Syndrome: Observations of Cases among Prisoners of War in Manchuria.** *Med. J. Australia.* 1946, Aug. 17, v. 2, No. 7, 232–4.

"1. The 'burning feet' syndrome is described as it occurred amongst prisoners of war in Manchuria.

"2. A gross disorder of the peripheral vascular system was the most conspicuous feature in the advanced cases of this syndrome.

"3. It is possible that these changes were the result of a disturbance of the autonomic nervous system, and aggravated by cold.

"4. The causal factor appears to be a deficiency of some part of the vitamin B complex."

WEINBERGER, E. Une épidémie de béri-béri secondaire au Kivu. [**An Outbreak of Secondary Beriberi at Kivu.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 256–60. [19 refs.]

Kivu is a district of the Belgian Congo. By the term " secondary beriberi " the author implies the condition known also as epidemic oedema ascribed to non-absorption or mal-absorption of vitamin B, though this is present in the food. Among the workers in the district some 300 cases were seen in 1941–42, nearly all of the Banya-Bongo tribe. No women or children were attacked during the outbreak, but a few isolated cases occurred among them a year later. The symptoms were oedema, polyneuritis, gastroenteritis and cardiac disturbance, in some ending in rapid death. Eight autopsies were carried out, but beyond pulmonary and hepatic congestion and dilatation of the right ventricle nothing very distinctive was found. No cause could be assigned. The best form of treatment proved to be reduction or exclusion of salt from the diet and the giving of hydrochloric acid with meals, together with intravenous injection of 10 cc. of 15 per cent. $MgSO_4$ twice a day for 2–4 days. The author records also that 0·3–1·0 cc. of " sulphurated oil, 1 per cent., intramuscularly once daily for 2–4 days brought about a spectacular improvement of the neuritis." [The composition of this oil is not given.]

During the first 6 weeks of the outbreak no preventive measures were undertaken and 68 new cases were seen ; during the next fortnight HCl was given with meals and NaCl removed from the diet and there were only 3 new cases and one relapse ; then for another fortnight no such measures were enforced and there were 36 new cases and 26 relapses. *H. Harold Scott.*

CASANOVA, Jean. Coeur et béri-béri. Etude clinique, électrocardiographique et radiologique d'après cent observations personnelles. [**The Heart and Beriberi. Clinical Electrocardiographical and Radiographical Study of 100 Cases.**] *Algérie Méd.* 1946, May–June, No. 3, 203–24, 4 pls. & 2 figs.

While the grosser manifestations of beriberi have been closely investigated the cardiac disorders occurring in this disease, although clinically severe, have been little studied. During the 1940 campaign in Southern Tunisia an epidemic of beriberi involving some hundreds of Senegalese troops afforded an opportunity for study of the heart lesions by daily clinical examination, by serial orthodiagrams and by the Boulitte portable E.C.G. apparatus. These men had already suffered from beriberi, chiefly of the oedematous type, in French West Africa ; and they became considerably worse under the conditions of climate, physical exhaustion and dietary deficiency obtaining in Southern Tunisia. Some relapses took the form of asthenia, slight nerve troubles and latent cardiac phenomena ; such were the least severe and were rapidly relieved by vitamin treatment. Others took the form of dry beriberi with severe progressive cardiac involvement, nearly always fatal in spite of treatment. The author, in company with the majority of writers, had associated cardiac complications with wet beriberi rather than with the dry form, which provided most of the material for his observations ; and he suggests that their severity in his cases might be due to the fact that these had previously suffered from wet beriberi, and had subsequently relapsed.

After a clinical description of the wet and of the polyneuritic types of cases encountered, the author states that in the dry form of the disease pulsation may be seen in the epigastrium, the jugulars, and the brachial arteries. The radial pulse is of the Corrigan type, full, bounding and excitable ; it is rapid, reaching 120 to 160 per minute, and the rate varied greatly during the day, often

without obvious cause, the slightest exertion raising it by 30 or 40 beats per minute; it took up to 22 minutes to return to its initial rate. Daily intravenous injections of atropine in 50 cases produced little effect. Digitalis increased the pulse rate and also aggravated the feeling of ill-health of the patients, so constantly that the author regarded it as a diagnostic test for beriberi. The action of vitamin B_1 given in various forms was very variable. In the wet form of the disease, when the oedema diminished rapidly the pulse rate diminished, and the electrocardiogram returned to normal if there were no disorder of conduction. This return to normal was also seen in early forms of the dry disease. In the dry disease of some months' standing, however, vitamin B_1 in prolonged and massive dosage failed to slow the pulse rate, as cardiac degeneration was established; but the heart size diminished if the patient was kept prone and well cared for. In the chronic dry disease the pulse slowed only in two patients, both of whom developed mild infective jaundice while under observation, and it quickened beyond the initial rate after the attacks subsided with the development of a progressive and fatal myocarditis in both cases.

In a table are recorded the blood pressures, the pulse rates, and the rapidity of return to normal of the latter after exercise, of 34 patients suffering from dry beriberi. These show that the blood pressures and pulse rate bear a constant relation. In the wet form the blood pressures were lower, and the differences between systolic and diastolic were less. The venous pressure was raised in 10 cases, selected at random, being from 18 to 20 cm. of water. The liver was not enlarged except in the terminal stages.

Heart irritability was evident as a simple tachycardia without arrhythmia; the sounds were accentuated, and systolic murmurs of inorganic origin were heard in all areas, a small systolic murmur being followed by a sharp second heart sound. In some cases gallop rhythm occurred.

Radiography of the chests of 60 dry cases with cardiac changes showed enlargement of the heart shadow, especially on its right side; and there was increased amplitude of the ventricular contractions with exaggeration of the pulsations in the ascending aorta and especially in the pulmonary infundibulum.

After reviewing the literature on the subject, the author records in some detail his own findings in numerous E.C.G. tracings from his cases, and reproduces a few examples of these as illustrations. From his studies he concludes that the increased rapidity of the cardiac rhythm in beriberi is of sinus origin; and the myocardial troubles affect the contractile power of the myocardium and interfere with intracardiac conduction. Disorders of rhythm and of tension are clinically manifest by marked cardio-vascular irritability.

The author discusses the factors governing the types of beriberi encountered in this group of cases, and finds that the Negro is much more susceptible to beriberi than the European; he is also more susceptible to heart disease. Early in the epidemic, deprivation of vitamin B_1 was abrupt, dysenteric disorders further increased it, and the wet cardiac type of beriberi was more common than the dry. Later the wet form disappeared to be replaced by the dry. Clinical experience indicates that marked polymorphism of beriberi occurs in the cardiac types of the disease. There are two extreme clinical types, one with generalized oedema and more or less marked cardiac involvement; and the other the pernicious dry form leading to early heart failure; all gradations between the two may be encountered; the dry form may become wet—but the pernicious heart involvement continues—and the wet form may become dry, when grave heart complications ensue.

The heart is affected by overwork and deprivation of vitamin B_1; this results in the wet form, where the heart rapidly shows its fatigue owing to obvious overload, but usually can rapidly be restored to normal by vitamin

therapy; while in the dry form of long duration, irremediable cellular changes occur, which affect the contractile power of the myocardium and interfere with its conductivity. *A. R. D. Adams.*

RUSSELL, Beatrice A. S. **Malnutrition in Children under Three Years of Age in Ashanti, West Africa.** *Arch. Dis. in Childhood.* 1946, June, v. 21, No. 106, 110–12, 1 fig.

This paper is a short account of a type of malnutrition in infants similar to, if not identical with, that described thirteen years ago by Cicely WILLIAMS, working in a different region of the same colony, under the name of kwashiorkor [see this *Bulletin*, 1934, v. 31, 344]. The features of the syndrome are oedema, irritability, muscular weakness and hypotonia, loss of tendon reflexes, depigmentation of the hair, dryness and "crazy-pavement" dermatosis, stomatitis, glossitis, diarrhoea, and anaemia. Dr. Russell makes the important observation that the general appearance may be most misleading, disguising the severity of the disease. Partly because of slight oedema, partly because it still retains subcutaneous fat, the baby looks plump rather than malnourished.

The history was usually that the child had been healthy until weaned at the age of 18 months or 2 years, when the next baby was born. Williams in her original description (*loc. cit.*) called this a "disease of the displaced baby." The onset is related to the diet after weaning, which in Ashanti consists mainly of maize, plantains, and cassava, and contains no milk.

The treatment recommended is a high protein diet. Pure vitamins were found to be of little value. Mercurial diuretics were used with good effect when the oedema did not disappear with dietary measures alone. At post mortem the liver was found to be fatty in two cases.

[It is unfortunate that a more detailed description is not given of the skin lesions, in view of the emphasis that has been laid on them by other workers (TROWELL, this *Bulletin*, 1941, v. 38, 722), and the controversy that has raged about their relationship to those of adult pellagra (STANNUS, this *Bulletin*, 1934, v. 31, 486; WILLIAMS, *Bulletin of Hygiene*, 1936, v. 11, 311; TROWELL, *loc. cit.*]

J. C. Waterlow.

GILLMAN, T. & GILLMAN, J. **Treatment of Infantile Pellagra. Assessment of the Value of Protein Hydrolysates.** *Lancet.* 1946, Sept. 28, 446–8.

The response to various forms of treatment of 161 cases of infant pellagra is summarized and illustrated in a table. The characteristics of this disease have already been described [see this *Bulletin*, 1945, v. 42, 748; 1946, v. 43, 59, 237]. The mortality is high (40–60 per cent.), and it is suggested that this is related to the presence of severe fatty infiltration of the liver, which is one of the typical features of the disease. By means of serial liver biopsies the authors were able to assess the response of the liver to different forms of treatment.

Supplements were given in addition to a basal diet adequate for infants and children. The most satisfactory results were obtained with dried stomach, 10 gm. daily (mortality 6 per cent.). After this the treatment of choice was by intramuscular injections of crude liver extract (10 ml. daily). The addition of pure vitamins to dried stomach, in the form of a preparation called "Ventron" (Parke Davis and Co.), or to liver extract given by mouth, appeared to increase the mortality. The worst results (mortality 78 per cent.) were obtained with pure vitamins alone.

Three types of protein hydrolysate were also tried. Two were casein digests, and one was a digest of whale-meat. In the trial of the first casein digest,

1 gm. was given 3 times a day : all the eight patients who received this treatment died. Two developed hyperpyrexia. The other digest was given in doses of 2–4 gm. per kilo. each day : one infant died, two deteriorated, and four recovered. This result was considered unsatisfactory. With the whale-meat digest three out of five infants died.

Since these protein hydrolysates failed to raise the plasma protein level and cure the oedema, it is suggested that the damaged liver was unable to utilize the protein breakdown products supplied to it. The authors consider that the success of the dried stomach is not due to the simple correction of a dietary deficiency. " Ventriculin is apparently able to cause such a radical alteration in the entire homoeostasis that the malnourished infant can now take advantage of the essential constituents of a good diet." [Homoeostasis is defined, in Dorland's Medical Dictionary, as a tendency to uniformity or stability in the normal body states of the organism.] *J. C. Waterlow.*

Kodicek, E., Carpenter, K. J. & Harris, L. J. **" Pellagragenic " Activity of Indole-3-Acetic Acid in the Rat.** *Lancet.* 1946, Oct. 5, 491–2.

Published work states that yellow maize yields from 20 to 100 mgm. of indole-3-acetic acid (heteroauxin) per kgm. : this substance is present largely in the form of a precursor that is readily converted by mild alkaline or enzymic digestion into the auxin.

Young rats given a diet of 3 per cent. cotton seed oil, 10·5 per cent. casein, 81·35 per cent. sucrose, 5 per cent. salt mixture, and 0·15 per cent. cystine with supplements of known vitamins except nicotinic acid, grew at a steady rate which was not significantly altered by the addition of either tryptophane or nicotinic acid. The addition to this diet of 1·5 mgm. indole-3-acetic acid per 100 gm. led to severe depression of growth in 19 of 32 rats. Of these 19 rats, 7 were then given also 1 mgm. nicotinic acid daily and 2 were given 20 mgm. tryptophane daily : these 9 rats resumed growth at approximately the same rate as the controls, while the remaining 10 rats did not recover. A similar effect was found in animals in the diet of which whole maize meal was substituted for 40 per cent. of the cotton seed oil, sucrose and cystine. Of 33 rats given such a diet, 29 showed severe depression of growth, which was restored in 4 by nicotinic acid and in 3 by tryptophane. When the protein in the diet was high (casein 20 per cent.) the addition of indole-3-acetic acid or maize meal had no apparent effect on growth. *H. E. Harding.*

Luckey, T. D., Moore, P. R., Elvehjem, C. A. & Hart, E. B. **The Activity of Synthetic Folic Acid in Purified Rations for the Chick.** *Science.* 1946, June 7, 682–4, 1 fig.

Day-old White Leghorn cockerels, under standardized environmental conditions, were maintained on a basal diet for three or four days, after which the effects of adding various accessory factors to the diet were observed over a further period of four weeks.

The addition of 25γ of synthetic folic acid prevented the reduced growth, poor feathering, and low haemoglobin and haematocrit values which resulted when the basal diet alone was given ; a similar though slightly less effect was obtained by the addition of 25γ of an isolated crystalline vitamin B_c in place of the folic acid. When vitamin C or whole liver powder was given with folic acid, growth was slightly better than with folic acid alone. The addition to the basal diet of 50γ of α-pyracin (2-methyl-3-hydroxy-4-hydroxymethyl-5-carboxypyridine), alone or with 10 or 50γ of synthetic folic acid, produced slightly better growth, but no improvement in feathering or haemoglobin ; 500γ of

α-pyracin alone added to the diet gave no response in growth, feathering or haemoglobin. No significant supplementary effect was noted with either *p*-aminobenzoic acid or a vitamin B_{10} and B_{11} concentrate in the presence of an adequate amount of synthetic folic acid. Experiments with vitamin B_{10} and B_{11} preparations without added folic acid demonstrated the lack of correlation between chick growth and microbiological activity.

When sulfasuxidine (succinylsulphathiazole) was added to the basal diet, the chicks developed a more severe deficiency, and under these conditions 25γ of synthetic folic acid did not give a complete response; further comparative tests indicated that folic acid was about three times as effective in the absence of the drug as in its presence, thus raising the possibility that folic acid acts indirectly to some extent. *F. Murgatroyd.*

SPRUE.

PAULLEY, J. W. & AITKEN, G. J. **Nicotinamide Methochloride Estimations in Sprue and Amoebiasis.** *Lancet.* 1946, Oct. 5, 486–7, 4 figs.

The authors used the method of COULSON *et al.* (1944) and ELLINGER *et al.* [this *Bulletin*, 1945 v. 42, 926].

For three days, 24-hour specimens of urine were collected from patients on ordinary hospital diet; for the next five days the same procedure was continued, save that patients were given 100 mgm. nicotinamide at the commencement of each 24-hour period. Each test lasted eight days. In 2 controls, 2 cases of sprue, 6 convalescent from sprue and 4 of amoebiasis, nicotinamide was injected parenterally. To the remainder—7 controls, 4 convalescent from sprue, and 3 of amoebiasis—the same substance was administered by the mouth.

The method of determining the amount of nicotinamide methochloride in the urine is as follows:—

Nicotinamide methochloride is separated from the urine by adsorption on "Decalso", from which, after washing with water, it is eluted by potassium-chloride solution, then rendered alkaline, and extracted with iso-butyl alcohol. The fluorescent derivatives thus produced are compared with standards by visual fluorimetry.

The control figures were found to agree with those of Ellinger *et al.*

Subnormal excretion, resting and after test dosage, was found in patients convalescent from sprue, who had had no symptoms for three months or more, and who had received nicotinic acid and liver treatment in India. Figures of excretion in this group were slightly higher than those of Ellinger *et al.* for pellagra.

The excretion in two cases of florid sprue did not differ from that in patients convalescent from sprue.

Whether nicotinamide was given orally or parenterally to patients convalescent from sprue and to controls, the level of excretion was similar. This indicated that poor intestinal absorption of the vitamin was not a factor in cases without intestinal "hurry". Patients with amoebiasis, either those with active disease, or those who were passing cysts, excreted less than the controls, but slightly more than the patients with sprue. Only two had diarrhoea, and both received nicotinamide parenterally.

The subnormal excretion in patients convalescent from sprue, who presented no symptoms and had received ample nicotinic acid during treatment, was surprising. Equally surprising was a similar deficient excretion in cases of amoebiasis.

It would be unwise to draw definite conclusions from these few results; a larger series is required.

It is suggested that behind this deficient nicotinamide-methochloride excretion in sprue and amoebiasis there may lie deficiencies of other members of the vitamin-B complex, known or unknown, whose relation to sprue may be of direct importance. *P. Manson-Bahr.*

MAEGRAITH, B. **Effect of Phosphate on Carbohydrate Absorption in Sprue.** [Correspondence.] *Lancet.* 1946, Sept. 14, 399–400.

The author refers to a preliminary communication [see this *Bulletin*, 1946, v. 43, 238] in which he and his collaborators reported experimental evidence that in active sprue there may be a failure of the phosphorylation of glucose at the time of its absorption.

In this letter, he reports on the effects of adding phosphate to carbohydrate solutions administered to cases of active sprue.

A patient with typical active sprue was subjected to an oral sucrose-tolerance test. The usual flat glucose and normal fructose absorption curves were obtained. This was confirmed by repeating the test by direct duodenal intubation of the sugar solution. Later, intravenous glucose produced a normal curve of disappearance of the sugar from the blood.

It was therefore presumed that the flat glucose curve was due to failure of absorption. The accessibility of the phosphate ion was investigated, in the belief that its exhibition, if phosphate was present in some inaccessible form, should restore the process of phosphorylation.

The sucrose-tolerance test was therefore repeated: the sugar was administered into the duodenum and 8 gm. of a mixture of potassium acid phosphate and disodium phosphate buffered at *p*H 7·0, was added.

The startling result was obtained that the glucose curve became normal but the fructose curve remained unchanged. A sucrose test made a week later without the phosphate once more produced the flat glucose curve. Some time later the sucrose plus phosphate test again resulted in a normal glucose curve.

Figures are given which demonstrate this finding strikingly.

In two of three other less active cases of sprue, phosphate appeared to assist the absorption of glucose.

Although the results are incomplete, the author suggests that in cases where glucose absorption is restored to normal in the presence of the phosphate ion, the latter might prove a valuable therapeutic agent.

H. J. O'D. Burke-Gaffney.

HAEMATOLOGY.

GIBSON, Q. H. & HARRISON, D. C. **Blood Haemoglobin: the Relationship between Oxygen Capacity and Iron Content of Blood in Men and Women.** *Biochem. J.* 1946, v. 40, No. 2, 247–9.

During previous studies on haemoglobin determinations it was found that the haemoglobin value of male blood, estimated by the oxygen capacity measurement, appeared slightly but consistently lower than that obtained from the determination of the iron content of the blood [see this *Bulletin*, 1946, v. 43, 773]. This fact had also been noted by other workers, who, however, unexpectedly found that in female blood the relationship was reversed. If there was, in fact, a systematic sex difference in the iron : oxygen ratio, there might also be a sex difference in the iron : colour and oxygen : colour ratios, and

different haemoglobin equivalents might be required for the artificial standard when used with blood from the different sexes. It was decided, therefore, to carry out parallel determinations of oxygen capacity and iron content on the blood of normal men and women.

Each oxygen determination was carried out in duplicate with the constant-volume van Slyke-Neill manometric apparatus, while the iron content was determined in triplicate by a modification of the method of Klumpp. Methaemoglobin was determined photoelectrically, and, where necessary, a correction was made to the observed oxygen capacity value. The haemoglobin determinations, using the artificial standard, were made according to the method described in the authors' previous paper, the samples being compared in a Spekker absorptiometer using Hilger-Chance OGr.1 green filters.

The results of examining 10 men and 10 women showed no difference in oxygen : iron ratio between the sexes. There was no difference between the sexes with regard to the ratio between iron and colour, or between oxygen and colour. The same haemoglobin equivalent may be used, therefore, for the standard in haemoglobin determinations in either sex. *F. Murgatroyd.*

VENOMS AND ANTIVENENES.

KIRK, R. & CORKILL, N. L. **The Venom of the Rhinoceros Viper *Bitis nasicornis* (Shaw).** *J. Trop. Med. & Hyg.* 1946, Feb.–Mar., v. 49, No. 1, 9–14, 2 figs. [17 refs.]

Bitis nasicornis is found in tropical Africa from Liberia to Kenya, especially near water and on ground liable to inundation. That captured by the authors was in the Imatong Mountains, Anglo-Egyptian Sudan, at a height of 6,500 feet and is said to be the first recorded from this district. Its venom is, apparently, less toxic than that of other species of *Bitis*, *e.g. B. gabonica*, *B. arietans*, *B. atropos* or *B. caudalis* (given by GRASSET, ZOUTENDYK and SCHAAFSMA as 0·4, 0·15, 0·3 and 0·3 mgm. respectively, as m.l.d. for mice [see this *Bulletin*, 1936, v. 33, 383]) and it does not really spit, like the spitting Cobra, *Naja nigricollis*, but the venom is ejected incidentally by contraction of the jaw muscles. A small amount only was obtained from this specimen but certain experiments were carried out with it. The m.l.d. subcutaneously administered to mice proved to be 0·5 mgm. ; intravenously a smaller dose was more rapidly fatal, but the authors had not enough venom to test this precisely. It had considerable spreading effect ; in fact, one of the most formidable complications of bites by this snake, if not fatal, is extensively spreading sepsis. The spleen, lungs and kidneys are found congested *post mortem*, and punctate haemorrhages are marked in the two latter organs. The spreading effect is due to a proteolysin, which was tested by Grasset and Schaafsma's method with different strengths of the venom on gelatin in saline. A haemolytic factor is also present, but it seems to be small in quantity and would have no practical effect on human beings bitten by this snake. It is suggested that the haemolytic factor, the spreading factor and the proteolysin may be identical [but the spreading factor is said to be great, while the haemolytic is but small]. Thrombase is not present in appreciable quantity. *H. Harold Scott.*

BINET, L. & WELLERS, G. Recherches sur le pouvoir antitoxique des composés sulfhydrilés. I. Action *in vitro* de quelques composés sulfhydrilés sur le venin de Cobra. **[The Antitoxic Power of Sulphydriles. I. *In vitro* Action of some Sulphydrile Compounds on Cobra Venom.]** *Bull. Soc. Chimie Biol.* 1946, July–Sept., v. 28, Nos. 7/9, 636–9.

VAN RIPER, W. **DDT and the Black Widow Spider.** [Correspondence.] *Science.* 1946, Aug. 2, 111.

When climatic and other conditions are favourable, houses may be inundated with collections of young Black Widow Spiders (*Latrodectus mactans*) which may grow to maturity and constitute a potential danger to young children. These pests are not susceptible to ordinary lethal substances, and they are very difficult to eradicate by individual hunting, owing to their retiring nature.

The author, in the Colorado Museum of Natural History, Denver, tested the effect of DDT on a mature female Black Widow Spider which was encouraged to make her web in a cigar box. A 10 per cent. solution of DDT in kerosene was sprayed very lightly on the outer part of the web, care being taken to avoid the spider and her retreat in the inner portion.

After 24 hours, she was seen half-way down the web, showing constant twitching movements of the legs. The next day she dropped from the web and was dead. Five additional spiders were placed in sequence in the same web, without additional spraying, and they all died in a couple of days.

The author is satisfied that a single spraying of the web of *L. mactans* with 10 per cent. DDT in kerosene is lethal to the spider and that the effect of spraying lasts for some time. *H. J. O'D. Burke-Gaffney.*

DERMATOLOGY AND FUNGUS DISEASES.

MONTESSORI, P. P. La granulomatosi coccidioide in Europa. [**Coccidioidal Granulomatosis in Europe.**] *Mycopathologia.* The Hague. 1941, Aug. 10, v. 3, No. 2, 131–9. [11 refs.]

Hitherto coccidioidosis has been regarded as a Californian disease; but of the four patients recorded here three had never been out of Italy and the fourth had never left Europe, nor, so far as is known, had any of them been in contact with a patient suffering from the disease. The cases referred to are :—

1. A girl of 14 years, living in Naples, recorded by BOERI and JACONO in 1929. She gave a history of cough for 7 years, with abundant sputum, at times haemorrhagic, bouts of fever, and, two years later, pleurisy which, however, soon cleared up, the other symptoms continuing in spite of all treatment. No tubercle bacilli were found, but a mycete was isolated and classed as Blastomycoides, and an intradermal reaction was obtained with a species of Cryptococcus. X-rays showed scattered shadows mainly about the hilum and a small cavity posteriorly at the level of the Vth vertebra.

2. A man of 40 years (in 1929) working in the Naples grain silos; symptoms similar and "Blastomycoides Castellani" is said to have been isolated. A study of this proved it to be identical with *Coccidioides immitis*.

3. A Neapolitan woman (in 1933) with gluteal swelling and later ulceration extending deeply, after local injection of camphorated oil. *Glenospora meteuropaea* isolated.

4. The same fungus isolated in 1936 by CASTELLANI from a Balkan patient in London. It was found to be closely allied to, but not absolutely identical with, *Coccidioides immitis*, and was named *C. immitis* var. *meteuropaeus*.

Experiments were undertaken by the author, using rabbits, guineapigs and rats, to compare *C. immitis* with *C. immitis* var. *meteuropaeus*. Intravenous injection of the latter into guineapigs resulted in a granuloma leading to death ; with rabbits death was very speedy with pulmonary granulomatous development. In rats, old cultures had no effect, but young cultures produced multiple inflammatory granulomata and the morphology was that of *C. immitis*.

A second experiment showed that the Neapolitan strain was the same as the Balkan, *i.e.* both were *Coccidioides immitis*. Next, the same three kinds of animals were inoculated with strains of the American *C. immitis*.

No real differences could be detected between the five strains. Any biological differences which were observable were slight, but perhaps sufficient to call the Neapolitan and Balkan strain *C. immitis meteuropaeus*, the Californian being *C. immitis typicus*. [But see below.]

Lastly, tests were made to see whether pre-treatment of guineapigs and rats with small repeated doses would set up a state of premunition or hypersensitivity to *C. immitis*, but no such change was detected.

It is concluded that the slight polymorphism of growth—character of the capsule and number of sporangia [these are not detailed]—in parasitic conditions are not enough to warrant conferring a new specific rank, or even variety, on the Neapolitan and Balkan strains. The main question is : Is the fungus found in these recorded cases autochthonous or has it been imported ? Three of the four patients lived in a coast town having ample communication with America and one worked with imported grain. Clinically, there are two points in favour of the European strain being biologically different from the Californian, namely, the relatively benign evolution of the former as compared with the latter, and its responding fairly readily to iodine treatment. The question of the autochthonous origin is left unanswered. *H. Harold Scott.*

Burks, J. W., Jr. & Thompson, P. E. **Coccidioidomycosis.** *Southern Med. J.* 1946, Aug., v. 39, No. 8, 613–20, 7 figs. [17 refs.]

A white American soldier, aged 27, who had recently served in California and the Arizona-Mexico border region, became ill with shortness of breath and palpitation. Three days later his temperature rose to 103°F. and a circinate, erythematous rash appeared on the extremities and the upper part of the trunk. There were no other signs or symptoms and the illness lasted only four days. Three or four weeks later a small blister developed on the upper lip and became crusted, and other painless, wart-like lesions, one to two centimetres in diameter, some with brownish crusts, appeared on the lip, nose, upper part of the back and lateral aspect of the thighs. The lip lesion resolved under X-ray treatment, but new lesions appeared on the nose, involving the left ala and the floor and septum, causing partial obstruction of the left nares by the projecting papillomata. The coccidioidin skin test gave a negative result, and microscopical examination of biopsy specimens from the nose yielded no positive evidence, but sowings from the same biopsy material on potato-maltose-agar and " Sabouraud's medium " gave a growth of *Coccidioides immitis* in 3 days at 37°C. A precipitin test with the patient's blood and *Coccidioides* antigen gave a negative result, but the complement-fixation reaction was positive to a titre of 1 : 32. These results, in conjunction, are taken as evidence of a severe coccidioidal infection, which might explain the failure of the coccidioidin skin test. Treatment by coccidioidin and penicillin injections was tried but the patient was killed in an accident before the effects of treatment could be determined. *J. T. Duncan.*

Silva, M. S. Tratamento da blastomicose sul-americana (granuloma paracoccidioídico ou moléstia de Lutz, Splendore e Almeida, blastomicose Brasileira). [**Treatment of South American Blastomycosis (Lutz's Disease).**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Nov., v. 2, No. 11, 918–27, 22 figs. English summary.

Paracoccidioidal granuloma, or the Lutz-Splendore-Almeida disease, to give its full name, is usually treated by oral administration of one of the sulphonamide drugs, sulphathiazole, sulphapyridine, sulphadiazine or sulphamerazine. Sulphapyridine is usually found too toxic. Another method is by vaporizing the drug on the oro-pharyngeal lesions and allowing absorption into the lungs from this; a third method is a combination of these two, oral administration and direct pulmonary administration by inhalation through the nose.

Details are given of seven patients so treated. Cough usually cleared in 2–3 days and "clinical cure" was obtained within a month, but the amount of the drug used varied within wide limits; one needed less than 50 gm. while another had 250 gm. It is necessary for the patient to be in hospital while this form of treatment is being carried out. *H. Harold Scott.*

Niño, F. L. Nueva observación de granuloma paracoccidioidico en la Republica Argentina. (Forma linfatico-tegumentaria). Estudio clinico y mycológico. [**Clinical and Mycological Observations on Paracoccidioidal Granuloma in Argentina. (Lympho-Cutaneous Type).**] *Mycopathologia.* The Hague. 1941, Nov. 10, v. 3, No. 1, 51–63, 4 figs. & 2 pls.

Girardi, V. C. & Khoury, C. Observación de pie de Madura en Buenos Aires. [**Observation of Madura Foot in Buenos Aires.**] *Rev. Asoc. Med. Argentina.* 1946, June 15, v. 60, No. 583. 487–90, 2 figs. [22 refs.]

Mycetoma is sufficiently rare in the neighbourhood of Buenos Aires to warrant the publication of a new case. The patient, a male Argentinian aged 22, had suffered for four years from an affection, of unknown origin, of the right foot, which was first noticed as a prominent but not sharply defined swelling on the dorsum, without local heat, redness, pain or any apparent involvement of the overlying skin. Six months later a sinus opened in the site of the swelling and discharged yellowish pus [no reference is made of the presence of "grains" in the pus]. The swelling extended progressively to the sole of the foot and the retromalleolar fossae and involved the whole dorsum anterior to the mid-tarsal articulation, causing much deformity. X-ray examination showed destructive changes in the cuboid and navicular bones and the earlier diagnosis of osteomyelitis was changed to the more specific tuberculous osteoarthritis. Rest and immobilization of the foot did not bring about improvement, and a biopsy examination was made which led to the new diagnosis of mycetoma caused by *Actinomyces madurae* [the parasitic grain of *A. madurae*, in the lesion, is sufficiently characteristic to be the basis of this diagnosis]. The patient was ordered intensive treatment with iodide of potassium and the local application of radio-therapy, but he returned to his home and his subsequent history is not available. *J. T. Duncan.*

van der Sar, A. & Hartz, P. H. **Mycetoma Pedis. Case Report.** Reprinted from *Amer. J. Clin. Path.* 1946, Feb., v. 16, No. 2, 129–38, 9 figs. [11 refs.]

Redaelli, P. Das Immunitätsproblem bei den Mykosen des Menschen. [**The Problem of Immunity in Human Mycoses.**] *Mycopathologia.* The Hague. 1943, Aug. 30, v. 3, Nos. 3/4, 280–309, 1 fig.

HEAT STROKE AND ALLIED CONDITIONS.

BURCH, G. E. **Study of Water and Heat Loss from the Respiratory Tract of Man. Methods : I. A Gravimetric Method for the Measurement of the Rate of Water Loss ; II. A Quantitative Method for the Measurement of the Rate of Heat Loss.** *Arch. Intern. Med.* 1945, Nov.–Dec., v. 76, No. 5, 308–14, 3 figs. [Refs. in footnotes.]

This relatively simple gravimetric method for the measurement of expired water is claimed to yield a mean accuracy within about 0·3 per cent. The inspired air passes through a meter to measure the ventilation rate. The expired air, as it leaves the subject's mouth, is heated to prevent premature cooling and condensing of the contained moisture. It then passes into a series of cooling coils where condensation occurs, and the water vapour can be collected. By weighing the coils, the weight of water condensed from a given volume of air can be determined. This is done also in a separate collecting system to measure the water-vapour content of the inspired room air. The collection of moisture from the inspired air of the subject is carried out for five minutes, while simultaneously an equal volume of room air is passed through the second circuit. The weight of water collected from the subject's respiratory tract represents the water inspired in the room air plus the water added during respiration. By subtracting the water contained in an equivalent volume of room air the water actually lost from the respiratory tract can be calculated.

The method and apparatus just outlined, with small modifications, enable the total heat loss from the respiratory tract to be measured and to be partitioned into its several components. Heat loss by evaporation of water is calculated by measuring the water loss as already described. To measure the heat loss due to warming of inspired air, the temperatures of inspired and expired air are measured by means of thermocouples ; since the mass of air inspired is known (the mass of water removed having been measured) and also its specific heat, the heat loss due to warming inspired air can be calculated. The third channel of heat loss from the respiratory tract is due to the decomposition from solution of carbon dioxide. This is measured by determining the subject's oxygen consumption, using a Benedict-Roth machine over a short period just after the previous observations ; the CO_2 output is then obtained, assuming an R.Q. of 0·83. Thus the total respiratory heat loss may be expressed as follows :—

$$H = h_e + h_c + h_{co_2},$$

where

H = Total heat loss from the respiratory tract.

h_e = Heat loss by evaporation of water from the membranes of the respiratory tract.

h_c = Heat loss by warming inspired air (convection) ; (this may be a positive number if air warmer than body is inspired).

h_{co_2} = Heat loss by virtue of the decomposition of H_2CO_3 in solution to CO_2 gas, which is expired.

The original paper gives details of the necessary calculations for each of the components h_e, h , and h_{co_2}. [There is a printer's error in this equation in the original paper, the + before h_{co_2} is shown as =.] *J. S. Weiner.*

BURCH, G. E. **Rate of Water and Heat Loss from the Respiratory Tract of Normal Subjects in a Subtropical Climate.** *Arch. Intern. Med.* 1945, Nov.–Dec., v. 76, No. 5, 315–27, 9 figs. [Refs. in footnotes.]

The respiratory water and heat loss of a large number of individuals living in a subtropical climate was measured under various conditions of room

temperature and humidity. Measurements on 56 subjects in comfortable surroundings showed little difference in respiratory water loss as between negroes and whites, male or female. The respiratory water output was highly correlated with the ventilation rate.

In cool dry or cool moist conditions there was no significant change in the total respiratory water loss. It was increased by a hot (50°C.) and dry (18 per cent. R.H.) environment and noticeably decreased in a hot (50°C.) and moist (49 per cent. R.H.) environment. The relative humidity of the expired air varied with the inspired air, the extremes being 78 and 97 per cent. In a comfortable environment the respiratory heat loss by evaporation was on average about 0·5 kilogram calories per square metre per ten minutes. This represents about 6 per cent. of the total loss of heat from the body and just over 50 per cent. of the total respiratory loss. The remainder of the respiratory heat loss is due to heat used in warming the inspired air—one-sixth of the total—and to heat absorbed by the liberation of CO_2 from solution—about one-third of the total. The total respiratory loss due to these three components represents about 11 per cent. of the total loss of heat from the body in comfortable conditions.

In cool conditions, heat loss by convection is somewhat increased. In hot, moist conditions, heat loss by evaporation is markedly reduced.

J. S. Weiner.

Pasquet, P. & Haulon, J. L'oedème cérébral dans le coup de chaleur et son traitement par le sérum glucosé hypertonique à 50 p. 100. [**Cerebral Oedema in Heatstroke. Treatment by 50% Hypertonic Glucose.**] *Rev. Méd. Nav. (Métropole et Outre-Mer)*. Paris. 1946, v. 1, No. 1, 9–14.

Intravenous injections of hypertonic glucose (25–50 ml. of 50 per cent. solution of glucose in " serum " [presumably physiological saline]) were given to eight cases of incipient heatstroke. There was immediate relief of symptoms, and the men were fit to return to duty after one or two days. The barest clinical details are given, and no mention is made of the condition of the skin, or of the presence or absence of sweating. None of the patients was hyperpyrexial; the highest temperature was 40°C. (104°F.). There was no loss of consciousness, although one patient was maniacal. Lumbar punctures were not made.

The treatment was based on the theory that the symptoms and signs—headache, dyspnoea, and tachycardia—are caused by cerebral oedema. The authors claim that the same method of treatment gives good results in more severe cases.

[In true hyperpyrexia it is a matter for argument whether the signs of central nervous system involvement are primary or secondary. They are usually preceded by complete cessation of sweating, and may be caused by the overheating of the body that results from the loss of evaporative cooling. A raised cerebrospinal fluid pressure is not always found on lumbar puncture. The cases described in this paper correspond more closely to those which have been called " heat exhaustion type 2 " by Ladell, Waterlow and Hudson [this *Bulletin*, 1945, v. 42, 143], except that in this condition there is usually diminution of sweating, with objective changes in the skin (scaling, lichenification). Fever, tachycardia, and dyspnoea are present, but respond rapidly to rest in bed alone.] *J. C. Waterlow.*

MISCELLANEOUS DISEASES.

FETTES, D. **Surgery in the Tropics.** *Practitioner.* 1946, Aug., v. 157, No. 938, 101–6.

In this short paper some of the pitfalls which await the surgeon who is a newcomer to the tropics are described. In general, the tropical surgeon must learn to adapt his methods to suit the climate and the habits and customs of his patients. That non-urgent surgery should be postponed till the cool season whenever possible; that Syme's amputation may give a more satisfactory stump in the case of Indian coolies than the modern methods which require an elaborate prosthesis; and that such patients require careful supervision to prevent them from tearing off their dressings or from getting out of bed immediately after a major operation, are lessons which must be learnt in the hard school of experience, unless they are inculcated beforehand. The reader is warned never to forget that malaria, typhoid and dysentery may cause acute abdominal symptoms, which may be mistaken for surgical conditions unless the surgeon remembers that in every doubtful abdominal case he should consider the possibility that he may be dealing with a purely medical complaint, that there may be a surgical complication of a medical disease present, or that there may be two diseases present. A careful history of the order in which symptoms appear, and a blood examination in every case, will save many mistakes. Early typhoid fever with pain and tenderness in the right iliac fossa may lead to a mistaken diagnosis and an unnecessary operation. The differential diagnosis between amoebic typhlitis and appendicitis may be difficult, and an operation may lead to haemorrhage and to the possibility of amoebic infection of any sinus which may develop. On the other hand, it must be remembered that a fulminating appendicitis may occur during the course of a severe attack of amoebic dysentery; and in such a case, if the history is correct for appendicitis, if the pain is of the severe type which indicates obstructive appendicitis, if a leucocytosis is present and if the case is early, an operation should be performed. In cases of more than 40 hours' duration, the Ochsner-Sherren treatment should be combined with the course of emetine. Amoebic granuloma is liable to be mistaken for carcinoma of the sigmoid or rectum and in all lesions near the anal canal the possibility of amoebic infection must be excluded by sigmoidoscopy, stool examination and a trial course of emetine before any operation is performed. Unrecognized hepatic abscess is responsible for more mistakes in diagnosis than any other tropical disease, and should be suspected in all cases of unexplained low fever, loss of weight and night sweats, when a malaria case is not responding to treatment; or if a patient is going downhill from no discoverable cause. Open operation for liver abscess is to be considered in patients who fail to progress after aspiration, emetine and chemotherapy, and for those in whom rupture through the lung has occurred; in pre-aspiration days it was possible to obtain good results by that method, even though the modern methods of preventing secondary infection were not then available. *W. L. Harnett.*

GHYOOT, E. L'appendicite chez les noirs. [**Appendicitis in Natives of the Belgian Congo.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1946, May, No. 5, 274–81. [17 refs.]

This is an English translation of the author's summary :—

1. Appendicitis is fairly frequent in Africans in the larger centres.
2. The clinical features are not well-defined, but tend to take the form of a collection of separate symptoms.

3. Appendix abscess is comparatively frequent and in some 30 per cent. of cases is the usual development of acute appendicitis.

4. Related peritonitis is not common, being seen in about 10 to 15 per cent. of cases.

5. Appendicitis is not confined to the more advanced natives of Léopoldville. It is found in more or less the same proportions amongst adult males in all classes. The rarity of the disease amongst females, and the fact that not a single case has been seen in children is noted, despite the frequency of helminthic infections in childhood, and the number of appendicitis-like symptoms reported in white children. *H. J. O'D. Burke-Gaffney.*

EARLE, K. V. **Pyrexia associated with Tick-Bite.** *J. Trop. Med. & Hyg.* 1946, Feb.–Mar., v. 49, No. 1, 14–15.

BROUWER, D. **Tropical Pyomyositis and its relation to Deficiency of the Vitamin-B Complex.** *J. Trop. Med. & Hyg.* 1946, Aug.–Sept., v. 49, No. 4, 77.

"In Java no evidence could be found that a vitamin-B deficiency played a rôle in the pathogenesis of tropical pyomyositis."

RANSFORD, O. N. **Tropical Myositis in East Africa.** *East African Med. J.* 1946, Sept., v. 23, No. 9, 278–84. [17 refs.]

GRALL, A. & GEYER, A. Deux cas de maladie de Kaposi chez le noir africain. [**Two Cases of Kaposi's Disease in Africans.**] *Méd. Trop.* Marseilles. 1945, July–Aug.–Sept., v. 5, No. 3, 207–18, 7 figs.

JHATAKIA, K. U. **Observations on "Eosinophilic Lung".** *Indian Med. Gaz.* 1946, Apr.–May, v. 81, Nos. 4/5, 179–84. [24 refs.]

The author analyses 140 cases of this condition seen by him during 1945. Patients were classed as suffering from "eosinophilic lung" who gave a history of asthmatic attacks or chronic cough, who had a leucocytosis above 10,000 per cmm., with eosinophilia over 15 per cent., and who had no other condition to which the eosinophilia might be due. All were residing in Bombay; 39 were working in grain-shops (inhalation of the dust of grain stores has been found as probable cause in a fair proportion of cases [? mites in the grain]); 106 were males, 98 adults, 8 children, and 34 were females, 4 of them children; 65 (46 per cent. of the total) were between 21 and 30 years of age, 30 (21 per cent.) were in their second decade, and 25 (18 per cent.) in the fourth. In 12 of the series there was evidence of allergy in some member of the family, and in 6 families more than one member was found to be a sufferer from the disease. The duration of illness varied within wide limits, between 16 days and 15 years. In one of those detailed the leucocytes numbered 63,450 per cmm. and eosinophiles 73 per cent. before injections of acetylarsen were started. In the laboratory findings the leucocyte counts ranged between 10,150 and 81,500 per cmm. and the eosinophil percentage between 15 and 90. The severity of the symptoms does not run *pari passu* with the blood count; the patient showing most distress had a leucocyte count of 12,000 and an eosinophilia of 18. Nor is the extent of the lung shadows proportional to the severity of the symptoms. Mites were looked for in the sputum of four only, and a single mite was found after prolonged search in one case. For treatment, the author mostly used acetylarsen, 6–8 injections of 3 cc. at three-day intervals. The causation is considered briefly—the histamine, allergic, parasitic, viral and spirochaetal theories—but no conclusion is reached. *H. Harold Scott.*

KESSLER, A. **Lathyrism in Man.** *Harefuah.* Jerusalem. 1946, Oct. 1, v. 31, No. 7. [In Hebrew 111–14. English summary 114.]

[A general account of so-called lathyrism, chiefly reiterating facts well known to readers of this *Bulletin* and to be found in all the best text-books on the subject.] The author states that this subject is acquiring increased importance in Palestine because inmates of a camp where the disease exists are finding their way into the country; he refers also to an outbreak in the Ukraine in which more than half the inmates (800 out of 1,400) of a camp were attacked. He gives a sketch of the symptoms which, he states, follow the ingestion of some 300 gm. of *Lathyrus sativa* (the chick-pea) for some weeks. [No reference is made to the fact that many authorities believe the symptoms to be due to poisoning by *Vicia sativa*, a weed contaminating the *Lathyrus*.] The symptoms are those of a developing spastic paraplegia and arterial spasm which may lead to gangrene of the toes. Remedial treatment by vitamins A, B_1 and D has been recommended and tried, but the results have not been promising. [The only effective treatment is removal of the cause and a careful outlook for the earliest symptoms—muscular cramps and frequent micturition. See this *Bulletin*, 1946, v. 43, 492, 787.] *H. Harold Scott.*

GRANA, P. C. **Conjunctivitis and Dermatitis due to "Beach Apple".** *Arch. Ophthalmology*, 1946, Apr., v. 35, No. 4, 421–2.

During manoeuvres in Panama in 1942 a certain company of an infantry regiment used branches of a local shrub as camouflage. Within an hour or two 13 men reported sick with dermatitis and acute conjunctivitis—erythema and swelling and vesication of the face and other parts touched by the hands, and blurring of vision, with profuse lachrymation. The shrub used was the manzanillo, Manchineal tree or "beach apple", which is common in the West Indies and in Central and South America. ALLEN has described it briefly in his work on *Poisonous and Injurious Plants of Panama* [see this *Bulletin*, 1943, v. 40, 724]. [The fruit is the more usual source of poisoning. This resembles a small apple, about an inch in diameter, and when bitten is pungent and irritating, causing smarting, salivation and soreness of the mouth, with vesication, ulceration and desquamation. All parts of the plant, however, are toxic; a latex exudes from leaves, branches and fruit when cut or bruised, and anyone sheltering under it from the rain may become affected.] The conjunctivitis is soon relieved by a boric acid wash and the skin irritation by a solution of bicarbonate of soda. [See this *Bulletin*, 1939, v. 36, 415; 1943, v. 40, 724, 863. A sketch of the plant is to be found in BYAM and ARCHIBALD's *Practice of Medicine in the Tropics*, Vol. 1, p. 778.] *H. Harold Scott.*

HEATHCOTE, R. St. A. **The Diamidines: their Pharmacological Actions and their Therapeutic Uses in some Tropical Diseases.** *J. Trop. Med. & Hyg.* 1946, Feb.–Mar. & Apr.–May, v. 49, Nos. 1 & 2, 1–8; 33–8. [109 refs.]

A useful and comprehensive summary of work published up to 1945.
E. M. Lourie.

GENERAL ENTOMOLOGY.

Olson, T. A. **Place of the Entomologist in Public Health.** *Amer. J. Pub. Health.* 1946, Sept., v. 36, No. 9, 1031–4.

Sautet, J. & Audibert, Y. Etudes biologiques et morphologiques sur certaines larves de moustiques en vue d'applications pratiques pour leur destruction. [**Biological Studies of some Mosquito Larvae in connexion with Methods for their Destruction.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 137–58, 9 figs. [19 refs.]

The first part of this paper has already been noticed [see this *Bulletin*, 1946, v. 43, 789]. This concluding part describes and tabulates the results of a large number of laboratory experiments made on the larvae of *Culex pipiens* and *Theobaldia annulata*, concerned mainly with the effect of temperature and suffocation on the rate of the cardiac rhythm in different instars. Other experiments record the effect of different antilarval substances.

Each experiment was conducted on a few larvae in small glass tubes, 1 cm. in diameter, and it was soon found that comparable results could only be obtained by observing larvae in the same stage of development because the cardiac rhythm rate varied with age.

In submerged larvae, the rate decreased more rapidly in fourth stage larvae than in second stage larvae and also slowed down more rapidly in warm water than in cold. The rate decreased until it reached a more or less constant value which was maintained for a short time by respiration through the anal and rectal papillae and the skin. The authors call this the "preagonic period". The "agonic period" begins when the cardiac rhythm becomes irregular both in frequency and intensity, after which death occurs. There is some indication that there is a threshold beyond which death occurs in any case whether treatment is continued or not.

Of the antilarval substances tested, calcium arsenite seemed to be most efficient for both species. *H. S. Leeson.*

Senevet, G. & Abonnenc, E. Les moustiques de la Guyane française. X. Le genre *Culex* (3). Nouvelle espèce du sous-genre *Culex*. [**The Mosquitoes of French Guiana. A New Species of the Sub-Genus** *Culex*.] *Arch. Inst. Pasteur d'Algérie.* 1946, June, v. 24, No. 2, 135–40, 1 fig.

Floch, H. & Abonnenc, E. Sur *A. nunez-tovari* et *A. pessoai* en Guyane Française. Table d'identification des *Nyssorhynchus* guyanais. [*A. nunez-tovari* **and** *A. pessoai* **in French Guiana. A Table for identifying** *Nyssorhynchus* **of Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 126.* 1946, May, 5 pp.

Wanson, M. & Lebied, B. L'habitat des Phlébotomes cavernicoles de Thysville (Congo Belge). [**The Habitat of the Cave-Dwelling Sandflies of Thysville.**] *Arch. Inst. Pasteur d'Algérie.* 1946, June, v. 24, No. 2, 153–6, 2 figs.

The cave-dwelling species of *Phlebotomus* (*P. gigas* and *mirabilis*) have already been described from a cave near Thysville, Belgian Congo. Both sexes of these have now been collected (revised descriptions are given elsewhere in the same number of this periodical). *P. gigas* is more frequently captured. The insects are found in a large chamber in an elaborate series of caves and passages, some 300 yards from the entrance of the cave, and therefore in complete darkness. *P. gigas* has also been found in another cave, near Matadi.

The sandflies never attack man, and will not feed on human blood in the laboratory. A precipitin test shows that some at least feed on bats (*Miniopterus*).

In details of structure of male genitalia the two species resemble certain American *Phlebotomus* rather than any others of the Old World.

A new *Anopheles*, *A. vanhoofi* has also been described from this cave [this *Bulletin*, 1946, v. 43, 1191]. The authors describe the caves, and refer to the remarkable cavernicolous fauna. *P. A. Buxton.*

PARROT, L. & WANSON, M. Notes sur les Phlébotomes. LIII. Sur *Phlebotomus gigas* et sur *Phlebotomus mirabilis*. [**Notes on Phlebotomus. LIII.** *P. gigas* **and** *P. mirabilis*.] *Arch. Inst. Pasteur d'Algérie*. 1946, June, v. 24, No. 2, 143–52, 9 figs.

PARROT, L. & HABIBI, A. Notes sur les Phlébotomes. LIV. Formes anormales de *Phlebotomus minutus* var. *parroti* Adler et Theodor. [**Notes on** *Phlebotomus*. **LIV. Unusual Forms of** *P. minutus* **var.** *parroti* **Adler and Theodor.**] *Arch. Inst. Pasteur d'Algérie*. 1946, June, v. 24, No. 2, 157–9, 3 figs.

FLOCH, H. & ABONNENC, E. Simulidés de la Guadeloupe : *S. antillarum* Jennings et *S. tarsale* Williston. [**Simulidae of Guadeloupe :** *S. antillarum* **and** *S. tarsale*.] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 130.* 1946, July, 6 pp., 2 figs.

GILLET, J. & WANSON, M. La lutte contre les mouches à Léopoldville. [**Fly Control in Léopoldville.**] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, Nos. 1/2, 55–80. [22 refs.]

Domestic flies are a serious nuisance in Léopoldville, and intestinal infections are very common. The authors report their observations on two species of fly which are abundant.

Chrysomyia putoria is very common and dangerous because it enters houses and sits on food [unlike most of the refuse-breeding species of *Chrysomyia*, we believe]. It will deposit eggs even in very dark latrines and pits, preferably in liquid excrement, contents of septic tanks, etc.

Musca cuthbertsoni (specimens determined by van Emden) is a widely distributed African fly. The eggs are laid in rather solid decomposing material, certain types of rotten fruit, excrement of man or horse, etc. ; liquefied materials, or very wet dung are not suitable. *Musca vicina* has been collected but is much less common.

The authors describe the breeding places of these two insects in detail, and show an intimate knowledge of local conditions. There are, for instance, storm water drains, not trapped nor designed to carry sewage : many domestic sewers have been connected to them illegally, and the drains then suit the *Chrysomyia*. There are also many septic tanks and squatting latrines without traps and therefore serving as breeding places. In general, the nature of the soil is important, for on a loose sandy soil many otherwise insanitary practices do not lead to the accumulation of liquids favoured by this fly. The construction of roads and buildings often leads, owing to lack of sanitation, to an outbreak of flies.

The authors have failed to find a cheap effective insecticide, which might be sprayed into breeding places of the *Chrysomyia*. Apart from familiar sanitary measures, some of which required structural modification of existing drains and the like, and are costly, the authors recommend trapping adult flies. They use what we should call a type of " Balfour trap " : large numbers of these traps exposed round markets, restaurants, etc., catch kilogrammes of flies per month. *P. A. Buxton.*

David, W. A. L. & Bracey, P. **Factors influencing the Interaction of Insecticidal Mists on Flying Insects. Part III. Biological Factors.** *Bull. Entom. Res.* 1946, Sept., v. 37, Pt. 2, 177–90, 5 figs. [13 refs.]

The spray cabinet used for the experiments in this investigation has been previously described [this *Bulletin*, 1946, v. 43, 679]. It was assumed that the activity of the insect in flying through a mist of insecticide would determine the quantity of poison accumulated on the body. This was confirmed in several ways. Mosquitoes (*Aëdes aegypti*) immobilized by light chloroforming and those with wings amputated were more resistant than normal insects; also, some batches of mosquitoes, which naturally displayed more activity than others, were more susceptible. Activity induced by mechanical stimulation increased the kill by insecticidal mist. Finally, a reversed experiment was performed in which the mist was moved at different rates over the mosquitoes (lightly chloroformed in a Buchner funnel). It was found that kill depended upon rate of movement of the air-borne mist sucked past the insects.

The kill of mosquitoes by mists of the insecticide DDT is largely influenced by the activity of the particular batch. Cyclohexanone, *Lethane 384* (n-butyl carbitol thiocyanate) and pyrethrins were all tested as activating agents to increase the effect of the DDT mist. Only the pyrethrins were effective and then at a non-lethal concentration.

Comparisons of the resistance of *Aëdes aegypti* adults of various ages showed a steady decline throughout adult life (from one to fourteen days old). This occurred both with DDT and pyrethrum and it was proved not to be due to increased activity in older adults.

The relative resistance of males and females was about equal at the beginning of adult life but thereafter the females were always more resistant. Females that had had a blood meal were more resistant than females fed on sugar and water and this was not merely due to sluggishness and therefore to accumulation of a smaller dose. The lack of water supply greatly increased susceptibility of both sexes. *J. R. Busvine.*

Herriott, R. M. **A Spectrophotometric Method for the Determination of p,p'-DDT.** *Science.* 1946, Sept. 6, 228–30, 2 figs.

The method depends upon two facts:—(*a*) ultra-violet absorption curves of solutions of para-para'-DDT and ortho-para'-DDT (the chief impurity of commercial DDT) both show low absorption at 250 mμ. The corresponding olefines of these two compounds, which are obtained by hydrolysis, show high absorption at this wave length. (*b*) Hydrolysis of para-para'-DDT proceeds much more rapidly than that of ortho-para'-DDT.

The procedure, therefore, is to compare absorption of alcoholic solutions of the unknown before and after a short period of hydrolysis, the difference indicating the para-para'-DDT content. The method requires a Beckman quartz ultra-violet photoelectric spectrophotometer. With dry deposits, etc., taken up by alcohol, an amount of 10 to 50 μgm. of p-p'-DDT may be estimated in ten minutes, but if the DDT is in kerosene (which also absorbs in the region of 250 mμ) the accuracy is diminished. [The wave lengths are given as above in mμ. and the weights as μgm.] *J. R. Busvine.*

Gunther, F. A. & Tow, Lois R. **Inhibition of the Catalyzed Thermal Decomposition of DDT.** *Science.* 1946, Aug. 30, 203–4, 1 fig. [14 refs.]

The presence of iron catalyses the decomposition (dehydrohalogenation) of DDT at high temperatures, and this may be responsible for much of the loss of active DDT from thermally generated smokes, etc., and possibly also from

residual deposits exposed to weathering. Two substances added to DDT at the rate of 2 per cent. have been found to inhibit this decomposition at 110–120°C. These are: Picolinic acid and salicylal-amino-guanidine. The efficacy of these in protecting residual deposits is under observation.

J. R. Busvine.

PIELOU, D. P. **Lethal Effects of D.D.T. on Young Fish.** [Correspondence.] *Nature.* 1946, Sept. 14, 378.

In Northern Rhodesia, deaths of young fish had been noticed after waters had been sprayed with DDT as an anti-mosquito measure; the author conducted experiments to determine the effect of larvicidal doses of DDT on the common and hardy Kafue "bream" (*Tilapia kafuensis*).

The first series:—Young fish, 1 in. long, were placed in pint jars of clear water, one per jar; 5·2 per cent. DDT in paraffin was applied in concentrations which were the equivalent of 1 oz., 0·5 oz. and 0·25 oz. of pure DDT per acre of water surface respectively; 100 per cent. mortality occurred in 24 hours, 72 hours and 120 hours respectively. Controls, using paraffin in like quantities, resulted in deaths on the tenth day, presumably from starvation.

The second series:—Similar experiments were conducted in 20-gallon aquaria with clear water, mud at the bottom, and very slight weed growth. At a dose equivalent to 1 oz. per acre the result was a 100 per cent. mortality in 24 hours; there were no deaths with a dose of 0·33 oz. DDT per acre. Attention is drawn to the difference in concentration of DDT per unit volume of water, DDT being very slightly soluble; 1 oz. of DDT per acre represents a concentration of 1 part DDT to 18 million parts of water in the first series, and 1 in 48 million parts in the second series.

The third series:—In natural pools, 40 sq. yd. in area and 2 ft. deep, produced by subsoil seepage and containing weeds from a muddy bottom and a rather heavy deposit of débris, no deaths were recorded until a concentration of 3 oz. DDT per acre (1 in 25 million) was used; this caused a 70 per cent. mortality in 4 days.

The author concludes that DDT should be used with great caution on waters known to be the breeding grounds of fish which are an important item of diet.

[LACKEY and STEINLE (this *Bulletin*, 1946, v. 43, 794) state that DDT in doses of 1 part per million is poisonous to *Gambusia affinis*, but that water thus treated becomes non-toxic in five days.] *R. Ford Tredre.*

DEWS, S. C. & MORRILL, A. W., Jr. **DDT for Insect Control at Army Installations in the Fourth Service Command.** *J. Econom. Entom.* 1946, June, v. 39, No. 3, 347–55, 2 figs.

In the early days of mobilization of the U.S. Army there were insufficient entomologists in the Sanitary Corps to deal with the pest insects and insect-borne diseases; but this was gradually remedied. Malaria was first attacked in the Fourth Service Command (headquarters Atlanta, Georgia), being a serious menace, because many of the reception areas were in or near swamps in highly malarious areas. Control measures included clearing, ditch cleaning and other drainage operations, as well as oiling. In 1942, 23 gallons [U.S. gallon=4/5 British gallon] of oil were used per acre in killing larvae. Later, in 1944, 15 gallons were found sufficient. Finally, DDT was applied at 0·2 to 0·3 lb. per acre in 3 to 5 gallons of oil; this saved much time and labour. The primary malaria rate in this Command was very greatly reduced in the years 1938 to 1943, but in 1944–5 there was a considerable increase, due to imported malaria.

A second objective was the improvement of barrack hygiene by destruction of bugs and cockroaches. At first, bugs were attacked with heat and pyrethrum or thiocyanate sprays; but these measures were only palliative. Later, HCN fumigation (6 oz. per 1,000 cu. ft., for eight to twelve hours) was introduced. When army operators were trained to replace men from commercial firms, the cost was reduced by about 70 per cent. Cockroaches were first controlled by powder containing pyrethrum and sodium fluoride. Later, DDT was introduced against both bed bugs and cockroaches, with great improvement as regards efficiency and duration of control, ease of application and cost. A 5 per cent. solution in kerosene was sprayed at the rate of about 1 oz. per sq. yd. For the roaches a 10 per cent. dust was also used with or without the spray.

Prior to the advent of DDT, fly control was carried out by spraying breeding areas with diesel oil No. 2 and the use of fly traps, etc. When DDT became available, it gave good results in the form of a spray (to walls, for residual effect) used in latrines, mess halls and also used to kill emerging adults on the breeding places.

Preliminary results show that DDT-proofing of timber will be a useful measure to prevent termite attack of buildings. *J. R. Busvine.*

KNIPLING, E. F. **DDT to control Insects affecting Man.** *J. Econom. Entom.* 1946, June, v. 39, No. 3, 360–66. [27 refs.]

As a result of extensive experimental work over three years, the use of DDT against certain insects affecting man has been developed to the point of provisional recommendations, as follows :—

Mosquitoes.

(*a*) Larvae.—For larvicidal use, 0·1 lb. DDT is used per acre, applied either in solution in petroleum oil, or in emulsion. This application must be repeated at intervals of one to three weeks, though a dose of 1–2 lb. DDT per acre remains highly effective for a month or longer. [The effect on fish, etc., does not seem to have been considered.]

(*b*) Adults.—For immediate action, the following formula can be used as an aerosol: pyrethrum extract 2 per cent. (0·4 per cent. pyrethrins); DDT 3 per cent.; an aromatic petroleum fraction (APS 202) 12 per cent.; "*Freon*-12" 83 per cent. For residual action a 5 per cent. kerosene spray or emulsion is used to give a deposit of 50 to 200 mgm. per square foot. For "area control", various sprays with droplets averaging 50 microns have been applied from aircraft at the rate of 0·1 to 0·6 lb. DDT per acre.

Lice.

(*a*) Body lice.—For rapid effective control, a 10 per cent. DDT dust (diluted with talc, pyrophyllite, etc.) is recommended. For persistent control, underwear should be impregnated by dipping in an emulsion or solution in "Stoddard solvent" [white spirit]. The underwear should be allowed to take up 1 to 2 per cent. of its weight of DDT, and this will last for six to eight launderings.

(*b*) Head lice.—The powder mentioned above is useful, but not always desirable. A less evident treatment is the application of the following liquid :—

Benzyl benzoate	68 per cent.	Diluted with five volumes of water before use.
DDT	6 „ „	
Benzocaine	12 „ „	
"Tween 80"	14 „ „	

Benzyl benzoate is included for its anti-sarcoptic value. Benzocaine is a useful ovicide; DDT does not kill eggs. "Tween 80" is an emulsifier (polyoxyethylene derivative of sorbitan mono-oleate).

(*c*) Crab lice can be eliminated by two treatments of DDT dust (with a week's interval between), or by one application of the above lotion.

Houseflies.

A residual spray to leave 100–200 mgm. DDT per sq. ft. should be employed in addition to continued attention to general sanitation and destruction of breeding places.

Fleas.

The dust and sprays recommended above are useful. One gallon of 5 per cent. DDT spray for each 1,000 sq. ft. of surface is suggested. On earthen floors, the dose should be increased.

Bed bugs.

DDT makes an ideal insecticide for this purpose at 5 per cent. in kerosene, or as an emulsion. About 3 gallons [U.S. gall.=4/5 U.K. gall.] are required to treat a large barracks (to hold 70 men). A coarse spray, such as that produced by an ordinary knapsack sprayer, is recommended. *J. R. Busvine.*

MINISTRY OF SUPPLY. **Some Properties and Applications of D.D.T.** 34 pp. [31 refs.] 1946. London: H.M. Stationery Office. [6*d.*]

EADS, R. B. **A New Species of Rhopalopsyllus Baker (Siphonaptera) from Texas.** *J. Parasitology.* 1946, Aug., v. 32, No. 4, 407–8, 1 pl.

STOCK, F. E. **Collapse of the Lung and Porocephalosis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Aug., v. 40, No. 1, 101–2, 1 pl.

Since the larva of *Armillifer armillatus* (*Porocephalus armillatus*) rarely produces symptoms, its presence is usually detected only at autopsy, although the parasite has been demonstrated during life in a few cases by radiography or during surgical operations.

The author describes what is believed to be the first recorded case in which pathogenic infestation with *A. armillatus* has been diagnosed during life.

The patient was a Nigerian native, aged 40 years, complaining of acute pain in the right chest, accompanied by fever. Clinical examination indicated X-ray examination; and this demonstrated complete collapse of the middle lobe of the right lung. At its hilum, there was a small "corkscrew-like" semicircular shadow, which was definitely a calcified nymph of *Armillifer.*

The patient recovered satisfactorily after treatment with sulphapyridine and breathing exercises. Three weeks later X-ray examination showed complete re-expansion of the lobe of the lung, but the shadow near the hilum remained unchanged.

The author considers that the lobar collapse may be attributed to the *Armillifer* infection, in the absence of other causes and in the presence of the calcified nymph in the immediate vicinity of the bronchus.

H. J. O'D. Burke-Gaffney.

LABORATORY PROCEDURES.

REIN, C. R. & BOSSAK, H. N. **Merthiolate (Sodium Ethyl Mercuri Thiosalicylate) as a Preservative in Sera for the Serodiagnosis of Syphilis.** *Amer. J. Syph.* 1946, July, v. 30, No. 4, 342–3.

This paper is abstracted in the *Bulletin of Hygiene,* 1946, v. 21, 812, and is of importance to serologists in the tropics.

Gómez Rodríguez, G. Valor del sulfato de zinc como fijador en técnica protozoológica y hematológica. [**The Use of Zinc Sulphate as a Fixative in Protozoological and Blood Work.**] *Bol. Asoc. Med. de Puerto Rico.* 1946, Mar., v. 38, No. 3, 95–7.

The author advocates the use of a mixture of an aqueous solution of zinc sulphate, two parts, and alcohol, one part, for fixation of blood films and faecal smears to be stained by Wright or Giemsa or iron haematoxylin. He claims that the methods he describes give results in a shorter time than do the usual procedures. [It is perhaps worthy of note that the solution of zinc sulphate is of the same strength as that employed in floatation techniques in which organisms may remain alive for a considerable time. One is led to wonder whether the fixation is due to the alcohol rather than to the zinc sulphate.]

C. M. Wenyon.

White, D. G. **A Hood to protect Precision Instruments in the Tropics.** *Trop. Agriculture.* Trinidad. 1946, June, v. 23, No. 6, 115, 1 fig.

Humid tropical atmospheres are notoriously conducive to producing corrosion of precision instruments and to the development of fungi which bring about etching of the glass in lenses.

The author gives an illustration, reproduced below, of a cellulose acetate hood, similar to those supplied by biological supply firms, but having certain further advantages.

The hood is made sufficiently high to include a microscope supported by a small wooden table, under which is a container of calcium chloride to maintain dryness.

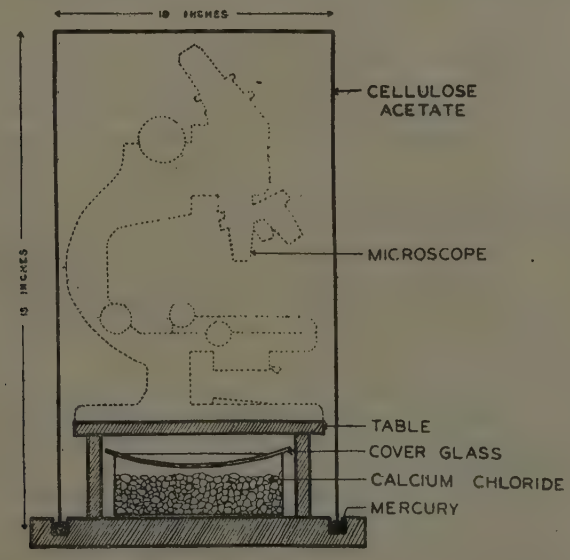


Fig. 1

Cellulose acetate hood for protecting precision instruments in the tropics.
[Reproduced from *Tropical Agriculture.*]

The edges of the hood are made air-tight by cementing with acetone: if small pieces of cellulose acetate are first dissolved in the acetone, warping will not occur.

The cylindrical shape of the hood is achieved by attaching three wire hoops to the inside with adhesive tape. The hood stands on a wooden base having a circular groove ¼ in. wide and ½ in. deep, containing metallic mercury, which forms an air-tight joint, but is not sticky like vaseline. This can be supplemented by rings of soft rubber hose tacked on each edge of the groove, which make a closely fitting additional joint into which the hood may be slipped. This type of seal is preferable where it is not desirable to have vaporized mercury in the laboratory. *H. J. O'D. Burke-Gaffney.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

SOUTH AFRICA, UNION OF: **Annual Report of the Department of Public Health for Year ended 30th June, 1944** [ALLAN, P., Secretary for Public Health]. 22 pp., 1 graph, 1945. Pretoria: Govt. Printer. [4*s.*]

The Department of Public Health, Union of South Africa, has had many difficulties to contend with in carrying out its duties, but much excellent work has been accomplished.

Health education and propaganda are aided by means of films, pamphlets, posters and charts for school use; this division is in the hands of the South African Red Cross Society. As elsewhere, there is a general complaint of lack of nursing staff and, towards the end of the year, a conference was held in an endeavour to find remedies for this shortage. The District Nursing Service has proved most valuable; its benefits are revealed in the reduced Infant and Maternal Mortality rates. In December 1935, there were 47 district nurses, in 1944 there were 533 employed. The Native Health Service does excellent work in antenatal and infant welfare; in the treatment of minor ailments at clinics and in visiting natives in their kraals. Nurses are stationed also at clinics where there is no resident medical aid. Where there are medical men available near schools the children are examined at least once a year and weighed monthly; health talks are given at frequent intervals and the children's homes are visited. But, by the time a child begins to attend school, he has, in many cases if not in most, already developed unhygienic habits; so, in Natal, a pre-school centre has been set up where instruction is given to encourage good habits, cleanliness, discipline, personal hygiene and physical training and games, proper feeding, etc. A number of Health Centres are to be established and £50,000 has been set aside for this purpose.

At the end of 1943 the total population of the Union was estimated as 10,788,500, of whom 2,265,000 were Europeans. Non-Europeans comprised 7,503,900 Bantu, 245,600 Asiatics and 874,000 "coloured" [these figures together come to 100,000 more than the total as stated]. The birth-rate among Europeans, 25·9 per mille, is higher than that of any other country except Portugal (26·1); England and Wales has 14·9. The death-rate, 9·5, is lower than that of any country except Holland (9·0) and New Zealand (9·4), that of England and Wales being 12·7. The European infant mortality rate was 47·31 per mille. There has been a steady decline since 1920 when the rate was 90·07 deaths per 1,000 registered live births. The I.M.R. in urban areas was 50·50 and in rural areas 40·83; it was higher among male infants (53·9) than among females (40·3). Diarrhoea and enteritis heads the list of causes of death,

accounting for 21·3 per cent., with bronchopneumonia second, 16·6 per cent. Still-births, were more than in the previous year 23·07 in place of 21·05 per 1,000 live births. The Asiatic infant mortality rate was 95·9 per thousand; among the coloured races there it was 153·27 per mille.

The Maternal Mortality rate in Europeans, was 2·85 per 1,000 live births; in Asiatics 6·06, and in the mixed and coloured races 5·1 per 1,000 live births.

As regards the death rate, figures for Europeans only are available and these not beyond December 1943. The figure, 9·53 per 1,000, is higher than in recent years, but lower than in 1937 (10·08). *Cardio-vascular disease* accounted for 22·3 per cent. of all deaths, 211·92 per 100,000, whereas in 1921 there were 103 per 100,000, or 9·9 per cent. of all deaths, attributed to this cause. The next commonest cause was *cancer*, which accounted for 11·5 per cent. of all deaths, 109·08 per 100,000. In 1921, only a little more than half this rate, 6·8 per cent. of all deaths, were so caused. The third in order, *pneumonia and bronchitis*, 92·23 per 100,000, also shows an increase. The *tuberculosis* death rate among Europeans, 33·16, is the lowest on record; in 1921 it was 58·26. This reduction is attributed by some to a drop in the cases of miners' phthisis. Figures for the Cape, Transvaal, Orange Free State, and Natal are given for males and females, for 1923 and 1943; from these it is seen that there has been a drop in all, except among males in Natal, where there has been a rise from 41·6 to 46·9 per 100,000. In the Transvaal the fall amongst males has been to less than half, from 74·45 to 36·52.

During the year under review there have been serious outbreaks of *typhus* and of *smallpox*. That of typhus was not, however, so severe as in 1920 and 1935. In 1944 there were 5,623 cases and 2,600 deaths, a fatality rate of 46·2 per cent. This outbreak was not quite so widespread as that of 1934–35, owing, it is thought, to the anti-typhus organization, the use of a mobile laboratory for obtaining information, to disinfection of clothing, inunction with naphthalene oil and injection of prophylactic vaccine. DDT was not obtainable from outside, so a local plant was set up for its manufacture; 30 lb. a month were made, and it is hoped than in 1945 as much as 500 tons will be manufactured. Typhus has been endemic in the Transkei for 50 years and this recent outbreak was limited to Transkei and Ciskei. Though the number of cases was less than in 1934 and 1935 the fatality rate was much higher (11·1, 14·5 and 46·2 per cent. respectively).

Smallpox occurred in 80 districts, affecting all four Provinces. Altogether there were 18 European and 1,028 non-European cases, and 71 deaths, all among the latter, a fatality rate of 6·8 per cent. The greatest number, 662, occurred in Natal. In this Province the disease had existed in a mild form for years, but in this outbreak it was of a much more virulent type, with a fatality rate of 9·3 per cent. (62 deaths).

Notifications have been higher than in 1943 for most infective diseases; exceptions were smallpox 1,046 (1,469 in 1943) and scarlet fever 2,237 (2,779). Cerebrospinal fever, 2,080, was more than doubled (931 in 1943), diphtheria 3,856 (3,417), acute anterior poliomyelitis 75 (36), puerperal fever 719 (565), tuberculosis 19,188 (17,136), and typhus 5,623 (2,879). Notifications of enteric (typhoid) fever have dropped from 3,917 to 3,486; the disease is commonest in the smaller towns where unhygienic conditions prevail. There were 839 European cases, 100 fatal (11·9 per cent.) and 2,647 non-European, 559 fatal (21·1 per cent.), but the figure is of deaths of natives registered in urban centres only.

Other diseases of which mention should be made are: Amoebic dysentery, leprosy, malaria, plague, schistosomiasis and tuberculosis. *Amoebic dysentery* was believed to be common, especially among non-Europeans, so an investigation was started in Durban and faecal examinations were made, with these

results: Of 975 Europeans 6·7 per cent. were positive; of 150 Indians 4 per cent. and of 375 Natives 36·0 per cent. These results, especially the figures for Indians, were unexpected and another 3,432 specimens were examined in Durban and South Natal, and this time the percentages positive were Europeans 5, Indians 3, Natives 17. Further study revealed that the chief cause was direct infection of food and milk by the hands of cyst-passers and, in native kraals, flies or contaminated water supplies.

There were 827 fresh notifications of *leprosy*. At the end of 1944 there were 2,398 lepers in institutions, 1,438 males and 960 females. Of the total, 563 were fresh admissions; 138 recrudesced, 227 had died and 347 had been discharged; 6,644 others were living in their own homes.

A short but severe outbreak of *malaria* occurred in Olifants River Valley. It started at the beginning of April, reached its maximum in 3 weeks, but lasted on till the second week in May. The vector was *A. gambiae*; the death rate could not be assessed accurately, but is believed to have been low. All passenger trains and motor-buses operating in or through malarious areas are sprayed regularly.

Plague has been less in evidence—62 cases (77 in 1943) and 39 deaths. Cyanogas dust and pumps are lent to farmers who make good use of them on their premises and progress is being made with rat-proofing farm buildings.

Schistosomiasis [the type is not stated, ? *haematobium*] is common among schoolchildren. Of 1,688 examined 15 per cent. were suffering from the disease, and in one school as many as 78 out of 108 examined. There is little to add to what has been said above regarding *tuberculosis*. Schemes for expansion in hospital and sanatorium accommodation have been approved, but this is only a "paper" advantage at present, because there are already 240 beds in existing institutions unoccupied, owing to shortage of nursing staff. When the schemes are in working order there will be 3,232 beds for the tuberculous, 724 for Europeans and 2,508 for non-Europeans.

The Dental Health Officer in a survey has examined 78,563 European schoolchildren and found carious teeth in 85 per cent. of them; 72 per cent. needed dental attention at the time. Disease was highest, 93 per cent., among children in urban areas, but even in rural areas it was 79 per cent. Among those with mottled teeth due to fluorine in the water the caries percentage was only 28.

There is a National Nutrition Council which has reported on nutrition surveys, on milk and milk products, certain foodstuffs, yeast, National School feeding schemes, rural malnutrition and other matters. Dietitians have been appointed and further nutrition and economic surveys are to be undertaken.

The poisoning of stock by algal growth in the waters of various dams, reported last year, has been eradicated by treatment of the waters with copper sulphate by means of sacks containing the salt towed by motor-boats. The sulphate is thus dissolved in a strength of one part in four million which, while destructive to the algae, was found to be harmless for man, fish and cattle. Constant observation, however, is called for, because the growths tend to recur.

H. Harold Scott.

Southern Rhodesia. **Report of the Public Health for Year 1945** [Martin, A. P., Medical Director & Chief Health Officer]. 61 pp. 1946. Salisbury: Rhodesian Printing & Publishing Co., Ltd.

Dr. Martin, having been Medical Director and Chief Health Officer for 10 years, takes this opportunity, in presenting his report of the work of the Public Health Department, of reviewing the conditions when he first assumed office and the work of the past decade. Fully half the period has been "war years" during which there was much dislocation of the service with a reduced staff

and the added duties of training medical and nursing units, and the treatment of the sick and wounded from the Abyssinian campaign. The Southern Rhodesian Medical Corps serving within the Colony comprised 7 medical officers, 8 dental officers and 150 " other ranks ". A central Medical Store for civil and military needs of the Colony was organized and has proved so successful that it will probably continue to be maintained in peace.

Readers will be interested in a few figures comparing 1936 with 1945. The European population has increased from 55,590 to 82,500 [but later, in a Table of Vital Statistics for 1945, the latter is given as 80,500], births in 1936 numbered 1,302, in 1945 they were 2,038, deaths 572 (687), infant mortality [presumably deaths] 64 (72), maternal deaths 9 (8), deaths from malaria and blackwater fever 66 (33). Europeans admitted to hospital have increased in number by more than 60 per cent. and out-patients more than threefold. Native admissions to hospital have risen from 12,328 to 29,498, " clinic " admissions from 11,744 to 66,758, and " mission " admissions from 8,838 to 22,393. At the same time Native out-patients have increased from 103,199 to 511,599. [Figures of increase such as these are often quoted to show improvement in the health conditions of a Colony, but they are of the nature of a two-edged sword. They are evidence of great increase in work done, but doubling or trebling the numbers of in-patients and out-patients is hardly evidence of improvement in the health of the people.]

Certain hospitals have been established or extended, partly by Government funds, partly by local subscriptions.

The native Clinic System calls for special mention. Prior to 1936 treatment of Natives was carried out largely at dispensaries, small in size and primitive in construction, scattered through the Colony. Now it is an " organised system, based upon the construction of specially designed buildings, in harmony with native ideas, but planned on a hygienic basis which allows the use of appropriate modern methods in the diagnosis and treatment of disease." In each area the main or central clinic is situated at the Station where the Government Medical Officer resides, and is surrounded by various sub-clinics placed at varying distances from it. At a main clinic the in-patient accommodation ranges from 40 beds in some places to 240 beds in others. Sub-clinics, which are mainly intended for out-patient treatment, nevertheless provide in-patient accommodation which varies in different places, and runs from 10 to 40 beds. These sub-clinics are visited by the Government Medical Officer as often as the need justifies ; some are visited twice a week, some once a week, and others once a fortnight ; serious cases are, for the most part, sent from the sub-clinic to the main clinic for treatment. Many of the stations already have their own ambulances, and others are in process of being provided with these vehicles as they become available for civilian use.

" Most of the main clinics carry out their own clinical laboratory examinations, the work being done by a trained African Microscopist. The clinics and sub-clinics are staffed and maintained by trained African Male and Female Nursing Orderlies, under the supervision and direction of the local Medical Officer."

At the end of 1945 there were 67 such clinics and requests are frequently coming in for more to be established. A large sanatorium is to be erected for the care and treatment of tuberculous natives ; it is hoped that this will be ready for occupation towards the end of 1946.

The Public Health Department is in a difficult and somewhat anomalous position in that it has to submit its affairs and proposals for approval by " an uninformed and non-technical Department of Internal Affairs " which prepares memoranda for submission to the authorities ; these memoranda may not agree with the demands of the Public Health Department but, nevertheless, they are not again submitted to that Department.

The report on 1945 is itself divided into five chapters dealing, in order, with Vital Statistics, Infectious and Communicable Diseases, Curative Services, Preventive Health Services and Administration, and there are 16 Appendices.

I. *Vital Statistics.*—The European population on June 30th, 1945, is estimated as 80,500 [but see above]; European births were 2,038, of which 86 per cent. took place in maternity homes; the birth-rate per 1,000 was, therefore, 25·3; deaths numbered 687, giving a crude death rate of 8·5 per 1,000; infant deaths, 72, give an I.M.R. of 35 per 1,000 live births; maternal deaths 8 show a M.M.R. of 3·9 per 1,000 live births. The chief causes of European deaths were: cardiac diseases 137 (20 per cent. of total deaths), cancer 94 (13·6), violence 73 (10·6), nervous diseases 51 (7·4), pneumonia and bronchitis 38 (5·5), malaria and blackwater fever 33 (4·8).

The Asiatic population was 2,970, "coloured" 4,280 and Natives 1,607,000.

II. *Infectious and Communicable Diseases.*—Dr. Martin states that notification is unsatisfactory and acknowledges frankly that the "figures are quite inaccurate." Bearing this reserve in mind we give a few of them: Chickenpox, measles, mumps, whooping cough, scarlet fever and diphtheria occurred in small numbers; smallpox occurred in 33 natives (all mild, none fatal) and pulmonary tuberculosis in 37 Europeans (4 deaths), and 299 Natives (70 deaths). Malaria is still the major cause of ill-health, but there has been no serious outbreak in recent years. Admissions to hospital for *malaria and blackwater fever* were the lowest since 1940—15 per 1,000 Europeans (24·7 in 1939, 27·3 in 1943); for blackwater fever, 15 Europeans were admitted and 4 died, 2 coloured and Natives, both died. The true figure for malaria is probably much higher, because those given do not include patients admitted to mine hospitals or to private hospitals, and many others treat themselves in their own homes and do not even call in a doctor. *Anopheles gambiae* is the chief vector.

For dealing with *schistosomiasis*, snail-infested waters were treated with finely-ground malachite ($CuCO_3$) mixed with an equal quantity of sawdust to which powdered *Swarzia madagascarensis* (3 per cent. by weight) was added. This contains a saponin and increases the solubility of the malachite. But 1,250 parts of the malachite per million of water (2,500 parts of the mixture) are needed to be lethal to the snails, and the mixture costs £10 a ton at Salisbury, whereas the sulphate has the same effect in a strength of 8 parts per million and costs £35 a ton. The latter, therefore, is more economical.

For patients a "fast treatment" has been adopted with success; injection of sodium antimony tartrate "12 mgm. per kilo of body weight given in six intravenous injections in two days." Injection must be slow, 5 minutes being taken to inject 2 grains of the drug in 10 cc. of glucose saline. Many have been thus treated and when examined 3 months later were not passing any ova. A further development is known as the "public health cure". Six grains are given to those weighing less than 120 lb., 8 grains to those over this weight. The dose is divided into three or four injections given in one working day. This kills the female worm and ends oviposition and thus achieves a "public health" cure. A skin test with antigen prepared from cercariae from living snails has proved of good diagnostic value, a reading being obtained in 15–20 minutes. The antigen is supplied free to medical practitioners. Free laboratory diagnosis is also provided and free treatment for schoolchildren up to 16 years of age. The infection rate is high; in some places Africans show an 80 per cent. incidence.

Human trypanosomiasis is endemic in the Zambesi Valley to the west of the common boundary with Northern Rhodesia and Portuguese East Africa. The vector, *Glossina morsitans*, occurs in the latter near the eastern borders of the Colony.

Leprosy.—Till 1944 lepers were housed in "pole and dagga" huts or in thatched Kimberley huts. Since then native leper villages have been constituted with a perimeter of brick cottages with tiled roofs and each with two single rooms. Within this perimeter are a communal kitchen, wash- and bathing-houses and an open-air Community Centre as a meeting- and dining-room. Each village is to accommodate about 100 patients. There are three larger leper institutions : Ngomahuru hospital, near Fort Victoria, takes both European and native cases, Mtemwa and the Mnene Mission take Africans only. At the first-named there were at the beginning of 1945 five Europeans, three coloured and 478 native patients. At Mtemwa there were 599 inmates at the beginning of the year ; at Mnene there were 29 on January 1st. During the quinquennium 1941–45 there were 1,149 fresh admissions and 314 re-admissions, a total of 1,463 (as compared with 1,503 in the preceding five years) ; 870 were discharged as cured or with the disease arrested, 286 had died in hospital and 128 had absconded. The true annual incidence of fresh cases for the five years, 1941–45, was 14·5 per 100,000.

In the same five years, 398 cases of *diphtheria* among natives were notified and 144 deaths (36·1 per cent., [not 28 per cent., as stated.]

European *pneumonia* cases numbered 378, of which 27 were fatal (7·1 per cent.) ; of 1,841 cases in non-Europeans 305 died (16·5 per cent.). *Typhoid fever* was not common, only 30 European cases were notified, 3 dying, and 65 among the Natives and coloured races, 10 fatal.

III. *Curative Services*.—There are 14 European hospitals, with X-ray plants at six. Native hospitals, with annexes for Asiatics and coloured races, number 13. European hospital admissions totalled 12,370 (13,410 in 1944) ; the reduction is ascribed to the temporary closing of some of the wards because of the critical nursing position. The *Nursing Service* is much below the establishment laid down, only 309 in place of 450, and there are only 91 qualified nurses whereas there should be 165 ; there are two sister-tutors instead of four. Many nurses are employed part-time and give good service. Sixty-one candidates sat for the Primary examination and 40 passed ; 17 presented themselves for the Final and all passed. There are 8 district Nurses, 4 at stations remote from doctors, and 6 have no hospital facilities ; 4 only are on the permanent staff. There are 67 *Native Clinics* built by natives under European direction. These are brick constructions with iron or tiled roofs and concrete floors. They are staffed by native medical orderlies and are visited weekly by a Government medical officer. In 1945 in-patients numbered 66,758 (64,192 in 1944) and out-patients 203,476 (181,162). A separate table gives the numbers of admissions and of out-patients attended at each of them. There are 34 *Medical Missions*. six of which employ doctors, the others being staffed by nurses ; some have Government grants-in-aid. Admissions numbered 22,193 (18,842) and out-patients 118,800 (97,218). The *Native Labour in Mines* is inspected and supervised. The average number employed during the year was 71,660 (75,155) ; deaths among these on account of disease numbered 7·84 (7·55) per 1,000 ; deaths from accidents 1·12 (1·09) per 1,000 ; deaths from pneumonia 2·18 (1·89). Cases of sickness totalled 37,675 (42,171) and of accident 16,932 (16,395).

IV. *Preventive Health Service*.—There are three important laboratories : the Public Health laboratories at Salisbury and Bulawayo and the Government Analyst's laboratory at Salisbury. Africans are trained to examine blood films for malaria parasites, stools for helminth ova and urines for schistosome eggs. For malaria and bilharzia the service is free.

There are two female and one male *school medical officers* and three Government *dental surgeons*, two at Salisbury and one at Bulawayo. The dentists examined 11,858 children and treated 1,471 of them. There are 10 qualified *health inspectors*, one public health inspector and 53 native vaccinators directly

supervised by the health inspectors. The St. John Ambulance and the Red Cross Associations have given good support to the hospitals and the former played a large part in the organization and planning of the blood transfusion services. Other facilities provided include free testing and immunization of children for diphtheria; free X-ray for fractures and bone diseases; free diagnosis of infectious and other diseases prevalent in the Colony; free radium treatment for cancer, and for venereal disease among natives. In 1938 a school for training of radiographers was opened at the Salisbury Hospital.

The appendices include a number of tabulated returns; detailed figures of the separate Native Clinics; a classification of deaths of Europeans; admissions and out-patient attendances at Government hospitals and at medical missions; returns from maternity homes; inspection of schoolchildren, records of work done, pathological, biochemical, etc., at the two general laboratories. Much of this has been embodied in the foregoing account. Finally, the Government Analyst's report gives the numbers of his examinations of water supplies, milks, foods, drugs, trade effluents, criminal investigations, toxicological and other forensic work. The report is of interest, not merely as a record of work done during the year, but in comparing the present conditions with those of ten years ago and telling of the progress during the decade. *H. Harold Scott.*

INTERNAT. LABOUR REVIEW. 1946, May–June, v. 53, Nos. 5/6, 340–48. **The Conditions of Indigenous Workers in the Belgian Congo in 1944.**

LAL, R. B. & SEAL, S. C. **The Teaching of Epidemiology in India.** *Indian Med. Gaz.* 1946, June–July, v. 81, Nos. 6/7, 261, 1 map & 3 charts.

The senior author has occupied, since 1934, the first chair of epidemiology to be established in India; he describes the course of training planned when he assumed office; this follows the same general lines as some of the modern courses of instruction in the U.S.A.

Field exercises are included in which surveys are made of conditions of life in Indian villages, and the students are called on to handle on the spot "mock" or real epidemics of such diseases as cholera.

In teaching the epidemiology of special diseases the method adopted is to deal with the general principles involved and then direct the students to acquire for themselves the knowledge of the measures suitable for the control of each disease. Guidance is given in the form of references or abstracts of the more important literature. The authors state that this method of study arouses the keen interest of the members of their classes.

Examples are given of the practical study in the field of three outbreaks of cholera.

The system adopted is undoubtedly sound; it aims at teaching the students how to learn for themselves, so that they may become "perpetual students", capable of keeping themselves abreast of all fresh advances in methods of controlling disease. *John W. D. Megaw.*

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ALPHABETICAL LIST OF AUTHORS OR SOURCES.

Adler, S. & Bichowsky, L., 52.
Agress, C. M., 33.
Allan, P., 138.
Amberson, J. M., 58.
American J. Hyg., 62, 67 *bis*, 68, 69.
American J. Hyg. Monographic Series, 20.
Andrew, R., 85.
Ann. Trop. Med. & Parasit., 27, 31.
Arch. Intern. Med., 28.

Baltazard, M., 92.
Bellerive, A. & Dambreville, C., 16.
Bengtson, I. A., 60, 61.
Bijlmer, J., 111.
Birnbaum, D., Goldblum, N. & Kligler, I. J., 22.
Black, R. H., 18.
Brackett, S. & Waletzky, E., with Baker, M., Hughes, C. O. & Williams, H., 40.
von Brand, T., Rees, C. W., Reardon, L. V. & Simpson, W. F., 84.
Brazzaville [A.E.F.], 45, 75.
Brennan, D. J., 115.
Brooke, M. M. & Proske, H. O., 22.
Brouwer, D., 129.
Buchanan, G., 93.
Bull. U.S. Army Med. Dept., 89.
Burch, G. E., 126 *bis*.
Burgess, R. C., 114.
Burks, J. W., Jr. & Thompson, P. E., 124.

Canaan, T., 85.
Cantrell, W. & Jordan, H. B., 39.
Carlson, H. J., Bissell, H. D. & Mueller, M. G., 39.
Casanova, J., 116.
Causey, O. R., Deane, L. M. & Deane, M. P., 20.
Cocalcaldi, J., 45, 75.
Chaudhuri, R. N. & Chauduri, M. N. R., 82.
Cheney, G. & Geib, W. A., 70.
Christianson, H. B., Gordon, H. H., Daniels, W. B. & Lippincott, S. W., 24.
Claessens, H., 49.
Cropper, C. F. J., 88.

David, W. A. L. & Bracey, P., 133.
Davis, D. H. S., 76.
Deane, H. W., 17.
Deane, L. M., Causey, O. R. & Deane, M. P., 20 *bis*.
Dews, S. C. & Morrill, A. W., Jr., 134.
Dimson, S. B. & McMartin, R. B., 32.
Dingle, J. H., 67 *bis*, 68, 69.
Dungal, N., 100.
Durand, P., Benmussa, S. & Caruana, M., 56.

Eads, R. B., 36.
Earle, K. V., 53.
Eeraerts, W., 49.
Epidemiological Information Bull. (UNRRA Health Division), Wash., 73.
Espersen, T., 100.
Etherington, D. & Sellick, G., 19.

Feinstein, M., Yesner, R. & Marks, J. L., 66.
Ferrebee, J. W. & Geiman, Q. M., 17.
——, Gibson, J. G. & Peacock, W. C., 17.
Fettes, D., 128.
Fischer, W. J. H., Jr. & York, C. L., 25.
Fletcher, D. E. & Rigdon, R. H., 42.
Floch, H., 53, 103.
——, Taillefer-Grimaldi, J. & de Lajudie, P., 93.
Franks, M. B., 107.

Gartrell, F. E. & Orgain, H., 20.
Ghyoot, E., 128.
Gibson, Q. H. & Harrison, D. C., 121.
Gillet, J. & Wanson, M., 132.
Gillman, T. & Gillman, J., 118.
Girardi, V. C. & Khoury, C., 125.
Glasgow, J. P., 47.
Gómez Rodríguez, G., 137.
Gouck, H. K., 78.
Grana, P. C., 130.
Gunther, F. A. & Tow, L. R., 133.
Guyane Française, 53, 103.

Halawani, A., Nor-el-Din, G., Shaker, M. & Khalek, F. A., 99.
Hargreaves, W. H., 80.
Hartz, P. H., 101.
Hayward, G. W., 81.
Heathcote, R. St. A., 130.
Henrard, C., Peel, E. & Wanson, M., 103.
Hernberg, C. A., 15.
Herriott, R. M., 133.
Hertzberg, R., 26.
Hill, K. R., 87.
——, Findlay, G. M. & Macpherson, A., 94.
Hitchcock, D. J. & Rawson, G. W., 84.
Hopkins, D. L. & Warner, K. L., 83.
Hughes, C. O. & Brackett, S., 41.

Jackson, C. H. N., 47.
Jacoby, H., 88.
Jhatakia, K. U., 129.
Jörg, M. & Aguirre, J. A., 115.

Kaplan, L. I., Read, H. S. & Becker, F. T., with Boyd, M. F., 25.
Kartman, L. & da Silveira, M. M., 88.
Kessler, A., 130.
Khalil, M. B. & Hilmy, I. S., 97.
Kirk, R. & Corkill, N. L., 122.
Kitchen, S. F. & Putnam, P., 23.
Knipling, E. F., 135.
Kodicek, E., Carpenter, K. J. & Harris, L. J., 119.

Lal, R. B. & Seal, S. C., 144.
Laurie, E. M. O., 76.
Levine, H. D., 59.
Luckey, T. D., Moore, P. R., Elvehjem, C. A. & Hart, E. B., 119

McCance, R. A. & Black, D. A. K., 44.
Macchiavello, A., 78.
Macfarlane, D. G. & Macy, R. W., 97.
Madsen, H., 110.
Maegraith, B., 121.
——, *et al.*, 27, 28, 31.
—— & Havard, R. E., 44.
Mahaffy, A. F., Smithburn, K. C. & Hughes, T. P., 72.
Manwell, R. D., 43.
Marsden, A. T. H., 86.
Martin, A. P., 140.
Monat, H. A. & McKinney, W. L., Jr., 90.
Montessori, P. P., 123.
Moorehead, M. T., 113.
Morris, K. R. S., 51.
Musgrave, A. J., 58.

Neujean, G., 56, 57, 58.
—— & Doucet, G., 57.
Noehren, T. H., 23.
Norman, A. P., 54.

de Oliveira, P. P., 96.
Oteiza Setien, A., Ibarra Perez, R. & Gonzalez Prendes, M. A., 95.
Oz, T. V., 59.

[*Continued Overleaf.*

ALPHABETICAL LIST OF AUTHORS OR SOURCES—*cont. from page 3.*

Pasquet, P. & Haulon, J., 137.
Peatley, J. W. & Aitken, G. J., 120.
Penfound, W. T., Hall, T. F. & Hess, A. D., 21.
Perry, J. S., 76.
Pielou, D. P., 134.
Pinto, C. & de Almeida, A. F., 96.
Planet, N. G., Cuocolo, R. & de Almeida, W. F., 90.
Ponce Caballero, L., 54.
Pratt, I. & Newton, W. L., 104.
Putnam, P. & Hackett, L. W., 15.

Quin, C. E. & Perkins, E. S., 92.

Radna, R., 94, 99.
Rafyi, A., 92.
Rail, G. A., 87.
Rajindar Pal, 19.
Rao, B. A., 16.
—— & Nassiruddin, M., 16.
Raynaud, R. & Pégullo, J., 93.
Reis, C. R. & Bossak, H. N., 136.
van Riper, W., 128.
Robbins, F. C., Gould, R. L. & Warner, F. B., 93.
—— & Ragan, C. A., 62.
—— & Rustigian, R., 65.
——, ——, Snyder, M. J. & Smadel, J. E., 64.
Rose, J. R., 86.
Rotenburg, S. S., 27.
Roth, H., 112.
Russell, B. A. S., 118.

Sarrouy, Combe & Claude, 55.
Saunders, G. M., Bianco, A. A. & Jordan, W. S., 108.
Sautet, J. & Audibert, Y., 131.
Seeler, A. O. & Ott, W. H., 41.
Selimkhanov, K. A., 91.
Sergent, Ed. & Sergent, Et., 36, 42.
Shih Lu Chang, 83.
Shute, P. G., 18.
Silva, M. S., 125.
Simeons, A. T. W. & Chhatre, K. D., 77.
Sinha, H. S., 86.
Sirtori, C. & Zorzoli, G., 85.
Smithburn, K. C. & Haddow, A. J., 71.
Spinks, A., 85.
—— & Tottey, M. M., 34.
Sprague, H. B., 25.
South Africa, Union of, 133.
Southern Rhodesia, 140.
Stock, F. E., 136.

Taliaferro, W. H. & Taliaferro, L. G., 40.
Tallant, E. J. & Maisel, A. L., with Rakestraw, M. R., 82.
Thompson, C. M. & White, B. V., Jr., 79.
Thompson, P. E., 43.
Topping, N. H., Shepard, C. C. & Huebner, R. J., 70.

Viswanathan, D. K., Rao, T. R. & Rao, T. S. R., 38.

Wanson, M. & Lebied, B., 131.
Watson, R. B. & Rice, M. E., 35.
Weinberger, E., 116.
Weller, T. H. & Dammin, G. J., 98.
Wenrich, D. H., 91.
Wharton, D. R. A., 106.
White, D. G., 137.
White, R. S., Ghosh, A. R. & Rao, V. V., 37.
Williamson, J. & Lourie, E. M., 48.
Wilson, D. B., 36.
Wird, K., 111.
Woodward, L. K., 79.

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